STUDIES OF ALTERNATIVE SOLVENT SYSTEMS TO RECYCLE PHASE SELECTIVELY SOLUBLE CATALYSTS

A Dissertation

by

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ABSTRACT

In recent years, the Bergbreiter group has investigated the synthesis and use of recyclable polymer-supported catalysts. If the polymer-supported catalyst has high phase selective solubility in certain solvents, the catalyst can often be separated from products with opposite phase selective solubility by using a biphasic separation. Thermomorphic systems, comprised of two solvents that are initially immiscible but that form one phase at elevated temperature, are used to run a reaction under homogeneous conditions and to separate the catalyst and the product in two phases afterward.

This work details the use of polymer-supported dyes as catalyst surrogates to examine the phase selective solubility of catalyst supports in thermomorphic systems and to study how leaching of polymer-supported materials into a product phase can be minimized. These studies include the synthesis of a nonpolar phase selectively soluble PIB-supported naphthol azo dye and its use as a catalyst surrogate to study leaching into the polar phase of a heptane/methanol thermomorphic system. It was found that leaching of the PIB-supported dye into the methanol phase was effectively minimized by the addition of nontoxic and nonvolatile poly(α-olefins) (PAOs) as cosolvents. Furthermore, when PAOs were used as a replacement for heptane, PAOs did not appreciably leach into the polar solvent when DMF or methanol were used.

The synthesis of a polar phase selective MPEG-supported dansyl fluorophore and its use as a catalyst surrogate to study the phase selective solubility of PEG supports in a heptane/DMF thermomorphic system is also described. The addition of MPEG as a

polymer cosolvent did not affect the leaching of PEG-supported dansyl dyes into heptane when PEG supports with molecular weights of greater than 1000 Da were used. Thus, MPEG could serve as a green cosolvent for this system.

Finally, the synthesis of a PIB-supported BINOL ligand is detailed. This ligand was prepared in a few steps and was tested in an *N*-arylation reaction. Although it showed very low reactivity in comparison with BINOL, similar PIB-supported ligands could be prepared and tested. The previous studies of alternative solvents can then be applied to the design of greener recycling systems for such polymer-supported materials.

DEDICATION

This dissertation is dedicated to my family, especially my parents and my grandmother, for their continual encouragement and support during my Ph.D. study.

ACKNOWLEDGMENTS

First and foremost, I would like to thank my advisor, Dr. David Bergbreiter, for his guidance during my Ph.D. study. He taught me that failure is not a tragedy as long as something can be gained from it. I also appreciate his willingness to help teach me the core principles of organic chemistry as well as how to solve problems when doing organic and polymer chemistry research.

I would also like to thank Dr. Jaime Grunlan, Dr. Daniel Romo, and Dr. Karen Wooley for their willingness to serve on my degree committee and for their valuable suggestions during my literature seminar and preliminary exam. I would also like to thank Dr. Lei Fang for his willingness to serve as a substitute for my final defense. I would like to thank Dr. Romo, Dr. Wooley, and Dr. Batteas for being excellent teachers who helped me to learn the deeper principles of organic, polymer, and surface chemistry when I took their courses. Additionally, I am grateful for the assistance of Sandy Horton and Jill Powers, who helped me immensely with the plans for my graduate study and far more. I would also like to thank Dr. Amber Schaefer, Dr. Holly Gaede, and Dr. Joanna Pellois, who were wonderful teaching mentors for me and who taught me so much.

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CONTRIBUTORS AND FUNDING SOURCES

Contributors

Faculty committee recognition

This work was supervised by a dissertation committee consisting of my advisor Dr. David Bergbreiter, Dr. Daniel Romo and Dr. Karen Wooley of the Department of Chemistry, and Dr. Jaime Grunlan of the Department of Mechanical Engineering. Dr. Lei Fang of the Department of Materials Science served as a substitute for Dr. Jaime Grunlan at my final defense.

Student/collaborator contributions

The PIB-supported azo dye phase selectivity project involved contributions from Ms. Coralys Torres-López and Ms. Kimberly Gonzalez, who did experiments under my supervision. Ms. Torres-López in particular studied PIB and PIB derivatives as anti-leaching solvents for thermomorphic systems. Mr. Thomas Malinski, a coworker in the Bergbreiter group, completed the synthesis of the PIB-bound *p*-methyl red dye and experiments of azo dye isomerization in the PAOs. Dr. Yannan Liang, a former coworker in the Bergbreiter group, synthesized the PIB-supported Rh(II) catalyst, conducted the cyclopropanation and O-H insertion reactions with this catalyst, and conducted anti-leaching tests with the PIB-supported ruthenium bypyridine complex.

The data for the PEG-supported fluorescent dye phase selectivity project was collected and analyzed in collaboration with Mr. Jonas Bianga, who was a visiting student

from the Technical University of Dortmund. Ms. Taylor Banks also completed experiments for this project under my supervision, in particular the synthesis of PEG-supported azo dyes and studies of their leaching in thermomorphic systems. All other work conducted for the dissertation was completed independently by me.

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CHAPTER I

INTRODUCTION

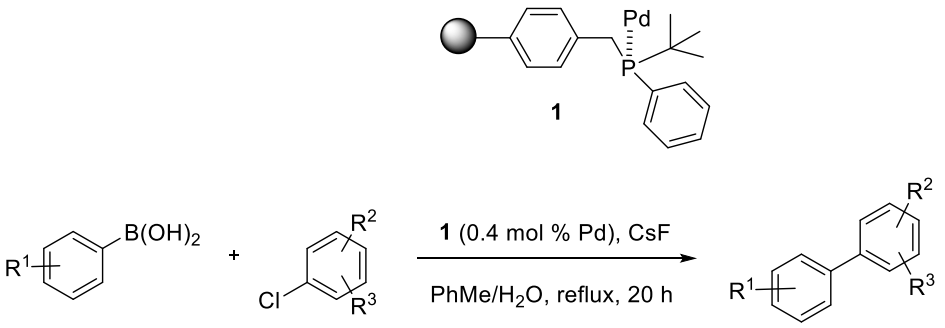
The development of new catalysts for chemical transformations as well as the improvement of older and more well-known catalysts will always be a fascinating and significant area of chemistry. Catalysis allows for the formation of new compounds and enables more efficient routes to well-studied compounds. Catalysis is one of the twelve core principles of green chemistry as catalytic amounts are always superior to stoichiometric ones.[1] However, catalysis is not without its inherent challenges, particularly with regard to sustainability. Often the products of catalytic reactions are difficult to separate from the catalyst itself, and require extensive purification techniques such as column chromatography to isolate the desired products. Such purifications can then require the use of volatile organic solvents, solvents which sometimes have undesirable toxicity or are not sustainable. These same issues are problems for catalytic reactions too, especially when homogeneous catalysts are used. Catalysts that contain metals can also leach these metals into the products of a catalytic reaction, limiting these products' further use due to unfavorable appearances or safety concerns. Because of these limitations, chemists have strived to make catalysis more sustainable, and have focused particularly on making the separation of catalysts from the product of a catalytic reaction greener and more efficient.

In the 1960s, Merrifield[2] and Letsinger[3] developed the syntheses of peptides and oligonucleotides using a cross-linked polystyrene resin. These revolutionary syntheses

used the insoluble polymer support to separate the intermediates in the syntheses from the reagents by a simple filtration. While the peptide or oligonucleotide intermediates were attached onto the resin, the reagents were removed by washing with solvent rather than the use of more time-consuming purification procedures such as recrystallization. After each intermediate was purified in this way, the reagents for the next step were added and the desired product was cleaved after the synthesis was complete. This separation strategy was later applied to catalysis where conventional homogeneous catalysts were attached to a modified heterogeneous support, such as the cross-linked polystyrene material Merrifield used.[4]

An example of a palladium catalyst with a cross-linked polystyrene support used for Suzuki-Miyaura reactions with aryl chlorides was reported by Becht and Le Drian.[5] This catalyst **1** was synthesized by the reaction of a disubstituted phosphine chloride with Merrifield resin followed by palladation with tetrakis(triphenylphosphine)palladium(0) to give a heterogeneous polymer-supported palladium catalyst that could be prepared on a 20 g scale. Catalyst **1** was used with 0.4 mol % of supported Pd to couple aryl chlorides with a variety of arylboronic acids using cesium fluoride as a base in toluene/water as shown in Scheme 1. Coupling reactions of phenylboronic acid with aryl chlorides containing electron-rich or electron-deficient substituents gave the products in >70% yield by ^{1}H NMR after 20 h. Most importantly, the catalyst was recyclable by a simple filtration in the coupling reaction of 4-chloroacetophenone with phenylboronic acid. Six subsequent cycles were completed with no noticeable decline in NMR yield, giving an average yield of 98% for the seven runs.

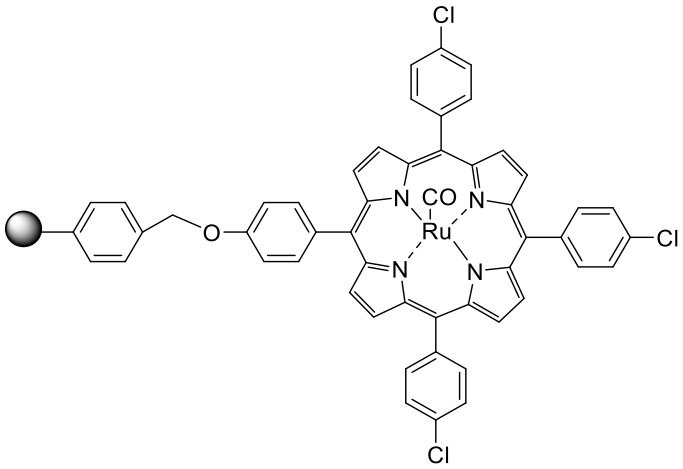
Another example of a catalyst with a cross-linked polystyrene support is a ruthenium-incorporated porphyrin catalyst used for alkene epoxidation reported by Che.[6] This catalyst **2** was prepared by the reaction of a ruthenium porphyrin with Merrifield resin and base to give the polymer-supported material shown in Scheme 2. Catalyst **2** with 0.005 mol % of supported Ru was used to carry out the epoxidation of styrenes with 2,6-dichloropyridine-*N*-oxide (Cl_2pyNO) in benzene to give the products in 86-94% yield by GC after 24 h. Cyclic alkenes such as cyclooctene or norbornene could also be used as substrates and the resulting epoxides were obtained in 98% yield. The reaction of styrene with Cl_2pyNO using catalyst **2** was repeated and the catalyst was recycled four times with no noticeable decrease in yield and an average GC yield of 92% was obtained for the five runs. Again, the catalyst could be recovered simply by filtration and drying.



Scheme 1. Suzuki-Miyaura reactions of aryl chlorides and phenylboronic acids with the polystyrene-supported palladium catalyst **1**.

Other than cross-linked polystyrene, silica is another commonly utilized heterogeneous support. Grubbs reported an example of a silica-supported catalyst for ring-

closing metathesis reactions in 2009.[7] This catalyst **3**, shown in Scheme 3, was prepared by the reaction of a triethoxysilyl-functionalized NHC ligand with base followed by addition of Hoveyda-Grubbs 1st generation catalyst; the Ru catalyst was then grafted onto silica by stirring at ambient temperature.



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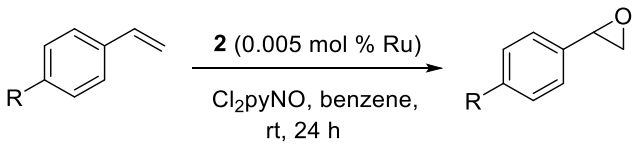
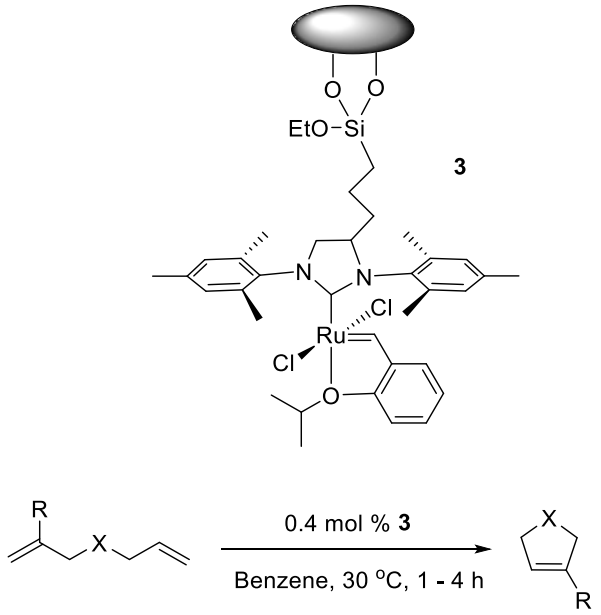


Scheme 2. Epoxidation reactions of substituted styrenes with the polystyrene-supported ruthenium porphyrin catalyst **2**.

The catalyst **3** (0.4 mol %) was then used for ring-closing metathesis reactions of substituted 1,6-heptadienes to give the resulting cyclic products with >80% conversion by ^{1}H NMR. The silica-supported catalyst **3** (0.75 mol %) was recycled successfully for the ring-closing metathesis reaction of diethyl 2,2-diallylmalonate. The average conversion

for seven runs was >70%. Recycling was carried out by filtering the reaction solution through a pipet containing steel wool to isolate the catalyst, which could then be reused in subsequent cycles.



Scheme 3. Ring-closing metathesis reactions of 1,6-heptadienes with the silica-supported Grubbs catalyst **3**.

As shown by these examples, heterogeneous catalysts are advantageous in that the separation of the catalyst from the products of a catalytic reaction is easily conducted by filtration after the conclusion of the reaction. This minimizes the need for further purification, and many heterogeneous catalysts can be recycled due to the ease of the separation of the catalyst from the reaction products. However, heterogeneous catalysts also have disadvantages compared with homogeneous catalysts. Heterogeneous catalysts'

reactivity and selectivity can differ from that of low molecular weight catalysts, and the reaction conditions may require modification to accommodate the insoluble support. While procedures exist to characterize these catalysts, many routine solution-phase characterization methods such as nuclear magnetic resonance (NMR) spectroscopy and UV-visible spectroscopy are not commonly used with heterogeneous catalysts.

Using soluble polymer supports to make recyclable homogeneous catalysts can address many of the challenges associated with using heterogeneous supports.[8] When using soluble polymer supports, a variety of strategies can be used to separate the catalyst from the product. Depending on the polymer support, different methods are used to accomplish this separation; these methods will be described in detail in the following section. Soluble polymer supports also have other advantages over heterogeneous supports for using, recycling, and separating catalysts. First, soluble polymer-supported catalysts are advantageous because their reactivity and selectivity are more predictable. Often the same reaction conditions can be used or the conditions can be easily modified to carry out catalytic reactions with soluble polymer-supported catalysts. Second, soluble polymer-supported catalysts can also be characterized more easily. In many cases NMR spectroscopy can be used to determine functionalization of the polymer support with the catalyst or to determine the polymer's molecular weight.

Preparation and Applications of Homogeneous Polymer-Supported Catalysts

A commonly utilized soluble polymer support for catalysis is poly(ethylene glycol), or PEG.[9] This is one of the oldest soluble polymers used for supporting and

separating catalysts.[10] It is prepared by anionic polymerization of ethylene oxide to yield a polyether which can be end-functionalized either with two hydroxyl groups or with one hydroxyl and one methoxy group (known as an MPEG). If an MPEG support is used, only one hydroxyl group can be functionalized with a low molecular weight catalyst. Two catalysts can be attached to each PEG support. PEG supports are commercially available in a variety of different molecular weights and are soluble in many different solvents such as water, acetone, dichloromethane (DCM), *N*,*N*-dimethylformamide (DMF), tetrahydrofuran (THF), and acetonitrile (MeCN). These supports' insolubility in other solvents such as hexanes, diethyl ether, and cold isopropanol also allows for separation of a PEG-supported catalyst from the products of a catalytic reaction by precipitation in these solvents, as illustrated in Figure 1.

One example of a MPEG-supported catalyst is 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), a catalyst for oxidation reactions that was reported by Pozzi and Benaglia.[11] This MPEG-supported TEMPO catalyst **4** shown in Scheme 4 was synthesized by the substitution reaction of a phenol-supported TEMPO with a MPEG support functionalized at one end with a mesylate group. Catalyst **4** (1 mol %) was successfully used for the oxidation reactions of linear, cyclic, and benzyl alcohols in DCM to the corresponding aldehydes using sodium hypochlorite as the oxidant. >95% GC yields were obtained within 30 min for most of the alcohols tested. The catalyst **4** was also recyclable for the oxidation of 1-octanol to 1-octanal using [bis-(acetoxy)iodo]benzene (BAIB) as the oxidant in DCM/water with a reaction time of 1 h and an average GC yield of 87% for seven cycles. However, recycling of **4** required precipitation into diethyl ether followed

by washing, which generated substantial solvent waste. About 10% of the catalyst was also lost during these cycles, which may explain a decrease in yield during the later cycles.

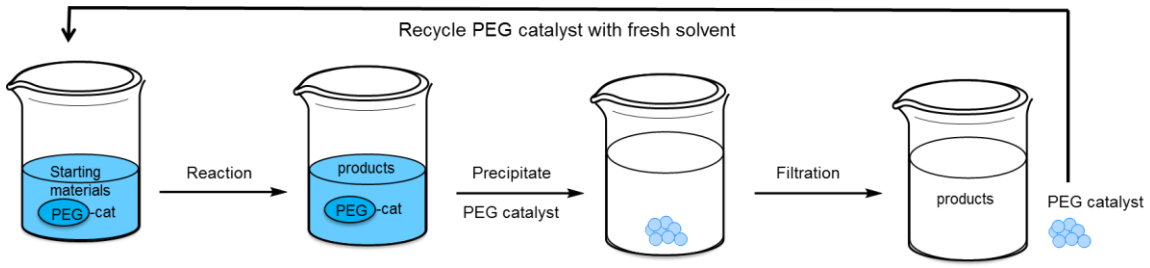
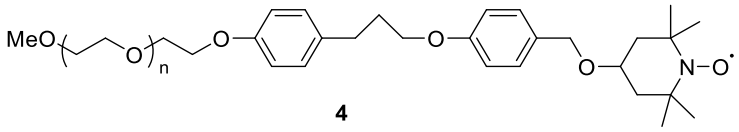
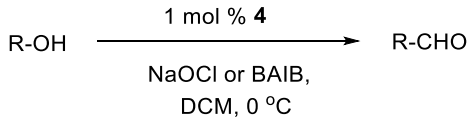


Figure 1. Typical recycling scheme for a PEG-supported catalyst.

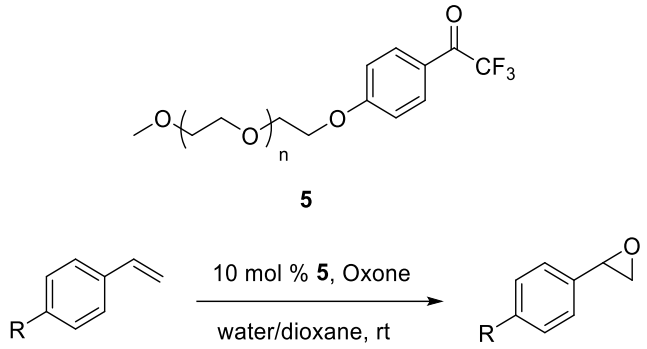




Scheme 4. Oxidation reactions of alcohols to aldehydes with the MPEG-supported TEMPO catalyst **4**.

Another example of a MPEG-supported catalyst is a trifluoroacetophenone precatalyst for epoxidation reactions that was reported by Toy.[12] This MPEG-supported trifluoroacetophenone precatalyst **5** shown in Scheme 5 was prepared by the reaction of mesylate-terminated MPEG with 2,2,2-trifluoro-1-(4-hydroxyphenyl)ethan-1-one,

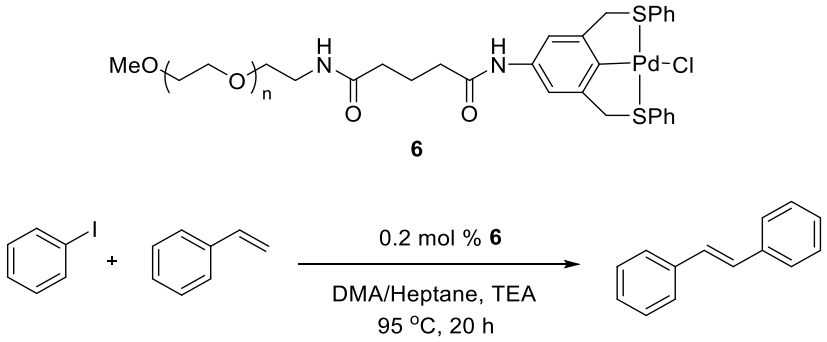
tetrabutylammonium iodide, and cesium carbonate. Precatalyst **5** (10 mol %) was then used to carry out epoxidations of a variety of alkenes and substituted styrenes in the presence of Oxone© in water/dioxane to obtain the epoxide products in >70% isolated yield after only 5 min. The catalyst could also be used for five cycles in the epoxidation of 4-vinylphenyl acetate, although 30 min was required for each cycle. The average isolated yield of the product for five runs was 83%, and the catalyst was easily separated each time from the reaction mixture by precipitation in diethyl ether.



Scheme 5. Epoxidation reactions of alkenes using the MPEG-supported trifluoroacetophenone precatalyst **5**.

Although soluble PEG-supported catalysts can often be recovered and reused, this recovery requires the use of substantial amounts of organic solvents for the precipitation and washing steps. The Bergbreiter research group proposed a greener way of recycling a MPEG-supported palladium pincer catalyst in 2000.[13] This MPEG-supported catalyst **6**, shown in Scheme 6, was synthesized in three steps starting with the reaction of potassium phthalimide with a mesylate-terminated MPEG. After attachment to the polymer support,

the MPEG-supported phthalimide was cleaved by reaction with hydrazine to give an amine. Coupling of the amine with a previously prepared carboxylic acid-terminated palladium pincer ligand using *N*,*N*-dicyclohexylcarbodiimide (DCC) gave catalyst **6**. This catalyst had previously been recycled by precipitation in diethyl ether,[14] but this work suggested the use of a thermomorphic system, a recycling scheme that is much greener and simpler to effect.



Scheme 6. Heck reaction of iodobenzene and styrene with the MPEG-supported palladium pincer catalyst **6**.

As shown in Figure 2, a thermomorphic system can be utilized when a polymer-supported catalyst and the products of a catalytic reaction have differing solubility.[15] In this case, the MPEG-supported catalyst **6** was soluble in 90% aqueous *N*,*N*-dimethylacetamide (DMA) while the products of selected Heck coupling reactions were soluble in heptane. 90% DMA and heptane are immiscible at room temperature, but upon heating to 95 °C they form one phase. Therefore, Heck reactions of aryl iodides with styrene or butyl acrylate using 0.2 mol % of catalyst **6** and triethylamine could be carried

out at elevated temperature for 20 h. After each reaction was complete, cooling to ambient temperature recreated a biphasic system where the products could be isolated from the catalyst by a simple gravity separation. The catalyst could be recycled for two runs by removal of the product-containing heptane phase and addition of fresh substrates and heptane to the aqueous DMA phase. These reactions showed low yields in the first cycle, probably due to partitioning of the product into the aqueous DMA phase containing the catalyst. However, for all of the substrates tested, product yields increased substantially for the following two cycles (>70% yield in cycle 2 and >98% yield in cycle 3).

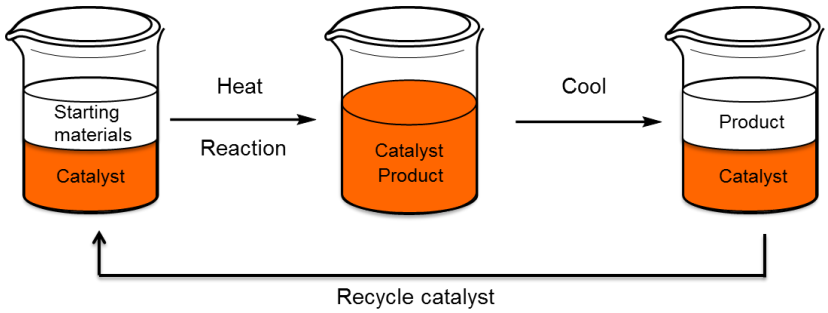


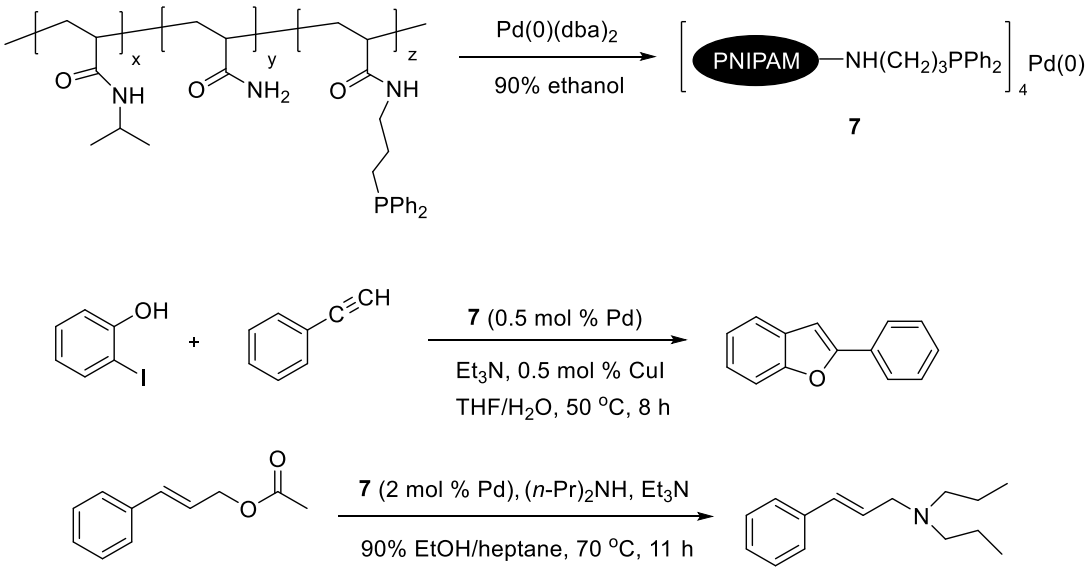
Figure 2. Thermomorphic solvent system recycling scheme for a PEG-supported catalyst.

Using thermomorphic systems to recycle phase selectively soluble catalysts can be extended to other polymer supports as well. Another example of a polar polymer support that can be used is poly(*N*-isopropylacrylamide), or PNIPAM. This polymer support is synthesized by free radical polymerization of the *N*-isopropylacrylamide monomer and can be copolymerized with other acrylamides to alter its properties, for example making

the support more hydrophilic or hydrophobic.[16] PNIPAM has a lower critical solution temperature (LCST)[17] of 31 ^{o}C in water, meaning that it will precipitate from aqueous solution at this temperature because of an unfavorable change in entropy. Initially below 31 ^{o}C, PNIPAM is dissolved in water and hydrogen bonding requires a certain level of organization of the open coil conformation of the polymer. Once the temperature reaches the LCST, PNIPAM precipitates because the ΔG free energy term changes from positive to negative due to a decrease in entropy, and the polymer will change from a soluble open coil conformation to an insoluble globular one. This precipitation is one method to separate a PNIPAM-supported catalyst from a reaction solution, but if the catalytic reaction does not work well in water, this can be a problematic separation technique. Many of the same thermomorphic systems that can be used with MPEG-supported catalysts can be applied to PNIPAM-supported catalysts as well, because PNIPAM has similar solubility in polar solvents (DMA, DMF, and aqueous ethanol) and insolubility in nonpolar alkane solvents like heptane.

The Bergbreiter group reported an example of a recyclable PNIPAM-supported palladium catalyst for Sonogashira coupling reactions[18] or for allylic amination reactions.[15] This catalyst **7**, shown in Scheme 7, was synthesized by free radical copolymerization of *N*-isopropylacrylamide and *N*-(acryloxy)succinimide followed by functionalization to attach an alkyldiphenylphosphine pendant group to a few of the acrylamide chains. This polyacrylamide then underwent palladation with bis(dibenzylideneacetone)palladium(0) to give the PNIPAM-supported palladium catalyst **7**. This catalyst (0.5 mol %) was then used for five cycles in the Sonogashira reaction of

2-iodophenol with phenylacetylene in THF/water at 50 °C using 0.5 mol % copper iodide. Catalyst **7** could be recovered by precipitation in water above the LCST or precipitation in hexanes, but recycling of this catalyst in this case was done using precipitation in hexanes. After the catalyst was recovered, it could be used again by adding fresh THF/water and substrates. A noticeable decrease in isolated yield of the product after 8 h was observed from the first cycle (78%) to the fifth cycle (58%), perhaps due to a mechanical loss of the catalyst as was noted with other precipitation recycling methods.



Scheme 7. Cross-coupling reactions with the PNIPAM-supported palladium catalyst **7**.

Alternatively, the same catalyst **7** could be used in the allylic amination reaction of *N*,*N*-dipropylamine with cinnamyl acetate in an aqueous ethanol/heptane thermomorphic system with triethylamine at 70 °C for 11 h. In comparison to the previous

study, this catalyst was recyclable four times and the product was obtained in high yield by separation of the heptane layer from the aqueous ethanol layer followed by solvent removal. Fresh substrates were then added in heptane to the catalyst-containing aqueous ethanol layer to recycle the catalyst. The average isolated product yield for five cycles was 95% but was 98% for the last four cycles, again showing the lower yield in the first phase (80%) was most likely due to partitioning of some of the product into the aqueous ethanol catalyst phase. This lower initial yield is disadvantageous, but can often be accommodated by high yields in subsequent cycles.

Another phase selective polymer support that can be used to modify catalysts is polyethylene (PE), which has temperature dependent solubility in solvents such as toluene, heptane, and THF. Initially at room temperature, PE is a waxy solid but upon heating to 70 ^{o}C the polymer dissolves in a solvent such as heptane to give a homogeneous solution. This allows for PE-supported catalysts to be used under homogeneous conditions and for the catalyst to be recovered as a solid after the reaction by cooling the hot solution to room temperature to precipitate the polymer-supported catalyst. Filtration and washing removes traces of products and often allows for the catalyst to be recycled easily.

Older and her coworkers at Dupont reported the use of a PE-supported porphyrin chain transfer catalyst **8** shown in Figure 3 for free radical polymerization of acrylates.[19] This catalyst was prepared by functionalization of a porphyrin backbone with mesylate-terminated PE followed by introduction of cobalt acetate dihydrate to form the metal complex. Catalyst **8** was used for the copolymerization of methyl methacrylate and *n*-butyl acrylate in methyl ethyl ketone (MEK) using 2,2'-azobis(2-methyl)butanenitrile as an

initiator to give polyacrylates with varying molecular weight (M_n) and dispersity (Đ) after 1 h depending on the mol % of the catalyst that was used. The prepared polyacrylates were light yellow to water-white in color, indicating that very little leaching of **8** into the polymer product occurred. In comparison, when low molecular weight porphyrin catalysts were used, the polyacrylates obtained were deep red in color, hindering their practical use. Catalyst **8** was used for ten cycles with no observed decrease in catalytic activity when separated by syringe filtration and centrifugation. Older and her coworkers described this catalyst as a "commercially viable" thermomorphic catalyst.

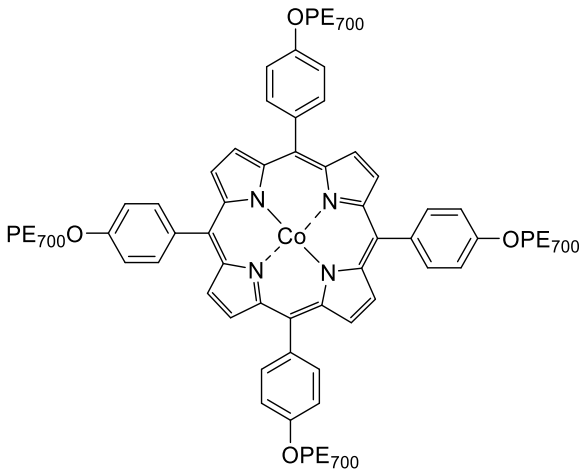


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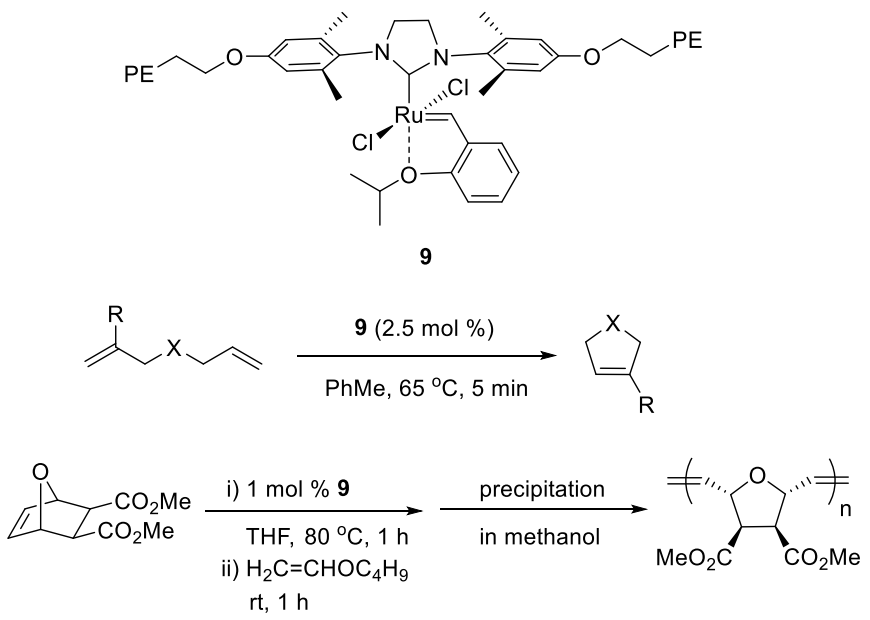
Figure 3. PE-supported cobalt-incorporated porphyrin **8** used as a chain transfer catalyst for the polymerization of acrylates.

The Bergbreiter group has also reported examples of PE-supported catalysts for use in metathesis reactions. In particular, PE-supported Grubbs catalyst **9** was used for

ring-closing metathesis[20] and ring-opening metathesis polymerization[21] as shown in Scheme 8. Catalyst **9** was synthesized by the reaction of an NHC ligand containing two PE oligomer chains with base followed by the addition of Hoveyda-Grubbs 1st generation catalyst.



Scheme 8. Ring-closing metathesis reactions and ring-opening metathesis polymerization using PE-supported Grubbs catalyst **9**.

Catalyst **9** (2.5 mol %) was first used for ring-closing metathesis reactions of 1,6-heptadienes in toluene at 65 °C for 5 min. The resulting cyclic products were obtained in 99% yield by ^{1}H NMR and the catalyst could be recycled eight times using *N*,*N*-diallyl-4-methylbenzenesulfonamide as a substrate with an average product yield of 96%. In these reactions, PE oligomers were added as a cosolvent. When the product was cooled down to room temperature after the reaction, these PE oligomers helped sequester the catalyst

and lowered leaching of the ruthenium metal from the polymer-supported catalyst into the toluene phase containing the products. This lower leaching was attributed to an "anti-leaching" effect due to the added PE oligomer cosolvent, a concept that will be further discussed in the following section when polymer solvents are introduced. The ruthenium leaching into the cyclic product formed from *N*,*N*-diallyl-4-methylbenzenesulfonamide was measured by inductively-coupled plasma mass spectrometry (ICP-MS) and <0.3% metal leaching was observed. This product was white, while the same product formed by using the low molecular weight version of catalyst **9** was obviously contaminated due to its grayish-green appearance. Reduction in metal leaching of the catalyst into the products is a notable advantage of using a PE-supported catalyst in comparison with its low molecular weight analogue.

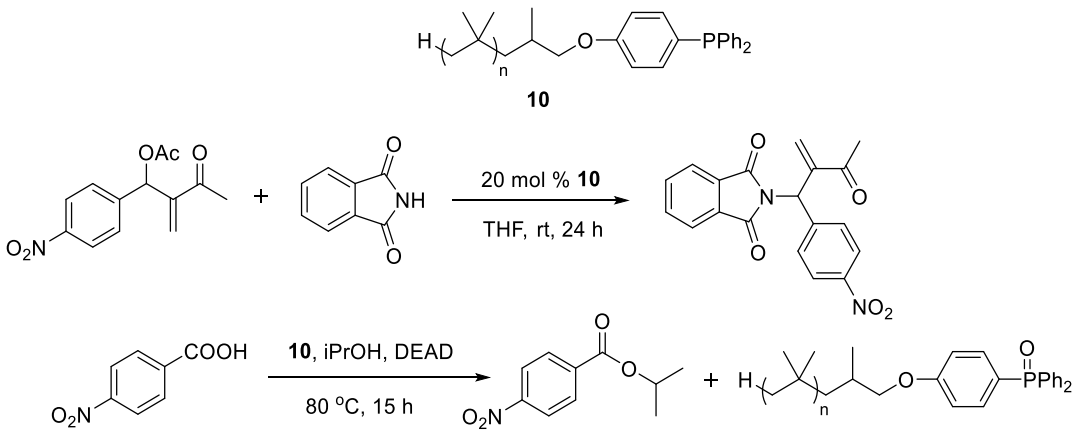
Catalyst **9** was also used in ring-opening metathesis polymerization of substituted norbornene derivatives, as shown in Scheme 8. These polymerization reactions were accomplished using 1 mol % of **9** in THF at elevated temperature for 1 h, followed by quenching with butyl vinyl ether and precipitation in methanol to obtain the resulting polymers with Đ values between 1.4-1.8 and a range of molecular weights. Again, polyethylene oligomers were used as a cosolvent to lower metal leaching into the products. As an example, the monomer shown in Scheme 8 gave a polymer product containing only 0.5% ruthenium (26 ppm) by ICP-MS when using the PE-supported **9**. Comparatively, when the low molecular weight catalyst was used to prepare the polymer product, 768 ppm of ruthenium was observed, a value that could only be lowered to 349 ppm after two additional precipitations in methanol were carried out, generating substantial solvent

waste in the process. These results further support the reasoning that the use of polymer-supported catalysts is an effective method to reduce metal leaching into products.

The polymer support that the Bergbreiter group has utilized the most in recent years is polyisobutylene (PIB), which is prepared industrially by cationic polymerization and like PEG is available in a variety of different molecular weights. In recent work in our group, PIB has been used as a polymer support for recyclable oxidizing agents,[22] nonpolar phase selective nanoparticles,[23] and for catalysts used in flow systems.[24] Because of its terminal alkene group, it can be easily functionalized with many different low molecular weight catalysts and its solubility in nonpolar and weakly polar solvents such as heptane, toluene, THF, and DCM and insolubility in polar solvents such as methanol, aqueous ethanol, DMF, and MeCN makes it an attractive candidate for use in thermomorphic systems or similar liquid-liquid separation systems. It has an additional advantage as a polymer support because it renders ligands and catalysts nonpolar phase selectively soluble. Because many catalytic reactions produce products with polar phase selective solubility, this nonpolar phase selective solubility creates versatility for the substrates that can be used. Unlike PE, PIB also has the advantage of being soluble even at sub-ambient temperature. PE oligomer ligands only dissolve on heating.

Although there are many examples that use PIB as a polymer support for catalysts or reagents, only two will be discussed here. The Bergbreiter group reported the use of a PIB-supported triphenylphosphine as a catalyst for allylic aminations and as a phosphine reagent for Mitsunobu reactions in 2011.[25] This catalyst **10**, prepared by the reaction of bromide-terminated PIB with 4-(diphenylphosphino)phenol, was first tested in the allylic

amination reaction of an allylic acetate with phthalimide at room temperature in THF for 24 h as shown in Scheme 9. After the reaction was complete, the THF solvent was removed under reduced pressure using a rotary evaporator and an equivolume mixture of heptane and MeCN was added. After separation of the two layers, the MeCN was removed under reduced pressure using a rotary evaporator and the product was recovered in 96% isolated yield after chromatography. The catalyst recovered from the heptane phase could be reused five times after the addition of fresh THF and substrates, giving an average isolated product yield of 87% for six cycles.

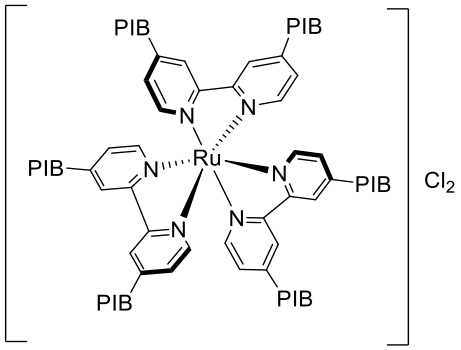


Scheme 9. Allylic amination reactions and Mitsunobu reactions using PIB-supported phosphine **10**.

The phosphine **10** was also tested as a reagent for Mitsunobu reactions using 4-nitrobenzoic acid, diethyl azodicarboxylate (DEAD), and isopropanol at room temperature for 15 h in THF as shown in Scheme 9. The triphenylphosphine oxide created from **10** could be separated from the product much more cleanly than the low molecular weight

compound by a simple extraction using heptane and MeCN. The product-containing MeCN phase was then purified by chromatography to give the product in 95% yield. The heptane solvent was then removed under reduced pressure using a rotary evaporator and the PIB-supported triphenylphosphine oxide that was separated could be reduced to **10** using trichlorosilane in toluene at 100 ^{o}C for 12 h. This result allows for the potential recyclability of **10**.

The Bergbreiter group also reported a PIB-supported ruthenium bipyridine photoredox catalyst for free radical polymerization of acrylates.[26] This catalyst **11** shown in Figure 4 was synthesized by the reaction of lithiated 4,4'-dimethylbypyridine with bromide-terminated PIB followed by the addition of ruthenium trichloride to form the complex. It was then used (0.01 mol %) for the polymerization of ethyl methacrylate using ethyl 2-bromoisobutyrate as an initiator with *N*,*N*-diisopropylethylamine in heptane at room temperature for 24 h. The corresponding polymer was obtained in 82% yield with a Đ of 1.2 and M_n of ca. 40000 Da.



11

Figure 4. PIB-supported ruthenium bipyridine catalyst **11** for the polymerization of acrylates.

The catalyst could be recycled two more times due to the insolubility of the polyacrylate product in heptane. As the reaction progressed, the polyacrylate product precipitated from heptane and the heptane layer was separated from the product. After the heptane layer was isolated, fresh monomer and reagents were added to repeat the polymerization. The average isolated product yield for three cycles was 78%, and ICP-MS analysis of the product polymer showed only 1.0 ppm of ruthenium contamination. This value was much lower than the 48.4 ppm result obtained when using the low molecular weight catalyst for the same polymerization.

Using soluble polymer-supported catalysts can solve many of the problems associated with low molecular weight homogeneous catalysts and avoids some of the problems encountered in using heterogenized versions of such homogeneous catalysts. Particularly, soluble polyolefin oligomer-bound materials like PE- or PIB-bound ligands and catalysts have reactivity that is analogous to their low molecular weight counterparts.[21,27] In addition, these catalysts are effective in lowering metal contamination of the products when an organometallic catalyst is used. Finally, recycling systems have also been developed for these soluble polymer-supported catalysts that allow for facile and green separation of the catalyst from the products of a reaction.

However, there are potential problems with the recycling systems used with these catalysts. First, when using a PE-oligomer bound catalyst, the PE-bound species can phase separate as a gel or as fine particles that make a physical solid/liquid separation challenging. Second, when using liquid/liquid separations with alkane and polar solvents, the extent of leaching of a ligand or a catalyst into the polar phase can vary depending on

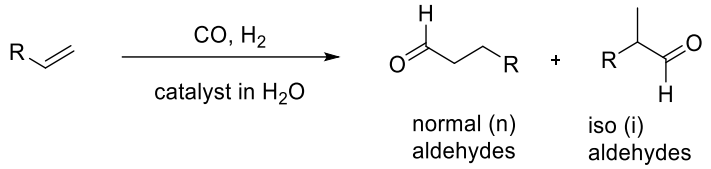
the relative size and polarity of the species bound to the polymer support. In addition, while this leaching is in general low, ligand or catalyst leaching into the polar phase can be an issue because then the catalyst is not fully recovered after the solvent extraction.

There are also other liquid-liquid recycling schemes that have been developed in the last few decades.[28] In some cases, these systems also use greener alternative solvents to replace toxic organic solvents. In other cases, they also include methods to facilitate recycling of the catalyst and separation of the catalyst from the products of a catalytic reaction.

Liquid-Liquid Recycling Schemes for Phase Selective Catalysts Using Alternative Solvents

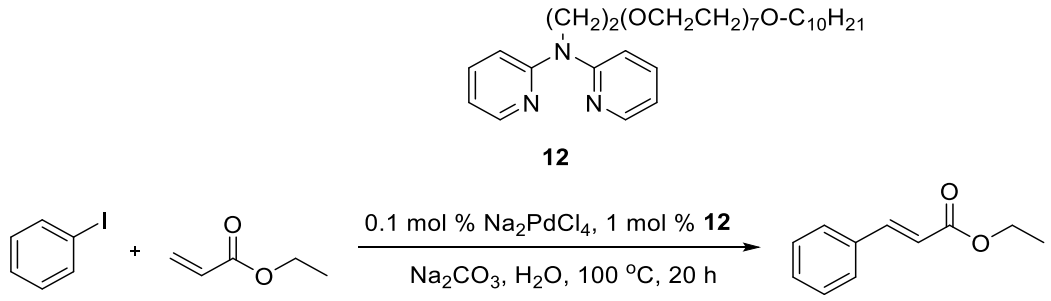
One of the most well-known and earliest studied liquid-liquid separation systems is based around water, an inherently benign solvent. Many organometallic catalysts with suitably polar ligands have solubility in water and aqueous biphasic systems can be used to separate these catalysts from the organic products that are formed.[29] In an aqueous biphasic system, the catalyst remains soluble in water while the product forms a separate phase or can be extracted using an organic solvent. For instance, aqueous biphasic catalysis has been used in industry for the hydroformylation of short-chain olefins, a process discovered at Rhône-Poulenc in the 1970s and further developed by Ruhrchemie a decade later.[30] This hydroformylation process uses carbon monoxide and hydrogen along with a water-soluble rhodium catalyst to give a mixture of *n*- and *i*- aldehydes as shown

in Scheme 10. In this case, the aldehyde products form a separate phase due to their insolubility in the catalyst-containing water phase.



Scheme 10. Hydroformylation reaction of short-chain olefins.

Larpent more recently reported the use of an aqueous biphasic system for Heck reactions using an amphiphilic dipyridyl ligand and disodium tetrachloropalladate.[31] The ligand **12** shown in Scheme 11 was synthesized by the reaction of *N*,*N*-di-2-pyridylamine with a bromide-terminated decyloctaethylene glycol. Ligand **12** (1 mol %) with 0.1 mol % of disodium tetrachloropalladate was then used to prepare a palladium complex *in situ* that successfully catalyzed the Heck reaction of iodobenzene and ethyl acrylate using sodium carbonate at 100 ^{o}C in water. After 20 h, the product was obtained in 89% yield. Recycling experiments were carried out by separating the product, which precipitated upon returning to room temperature, from the aqueous phase. Fresh substrates and base could then be added to the aqueous solution and the catalyst and ligand could be recycled twice more giving an average product yield of 89% for the three cycles. A substantial loss in activity was then observed with a yield of only 10% in the fourth cycle. It was also necessary to use a 10:1 ratio of the ligand to the catalyst to maintain a high yield of the product in the first three cycles.

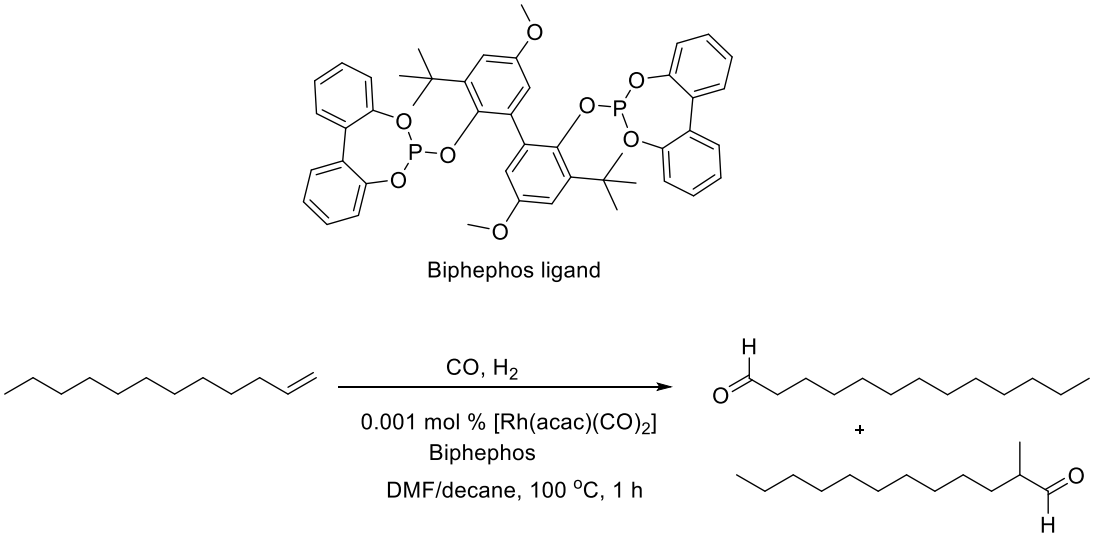


Scheme 11. Amphiphilic dipyridyl ligand **12** used for Heck reactions in an aqueous biphasic system.

Behr also reported a temperature-controlled multicomponent solvent system (TMS) of DMF and decane for the hydroformylation of 1-dodecene using a Biphephos ligand with (acetylacetonato)dicarbonylrhodium(I) as shown in Scheme 12.[32] Similarly to a thermomorphic system, the TMS system of decane and DMF is immiscible at ambient temperature but forms one phase upon heating. This allows for the products to be separated in the decane layer after cooling, while the catalyst can be recovered and reused in the DMF phase. Recycling of the rhodium catalyst after the hydroformylation reaction using carbon monoxide, hydrogen, and 0.001 mol % catalyst (0.005 mol % ligand) was quite successful, with product yields of 80% after 1 h obtained for the first thirteen cycles. The catalyst could be reused thirty times, although the yield decreased in later cycles unless the reaction time was increased.

Not surprisingly, the chain length of the nonpolar TMS component had an effect on the leaching of the catalyst into that phase. When hexane was used as the nonpolar component, the catalyst leached five times as much into the nonpolar solvent phase as when decane was used. If hexadecane was used instead of decane, the leaching was further

reduced by a factor of 2. The chain length of the alkene substrate was important as well, because if the chain length was too long an increase in leaching of the catalyst into the decane phase was observed. This result suggests that when using liquid-liquid solvent systems to recycle phase-selective catalysts, the substrates and their phase selectivity need to be carefully considered as well as the catalyst's phase selective solubility.



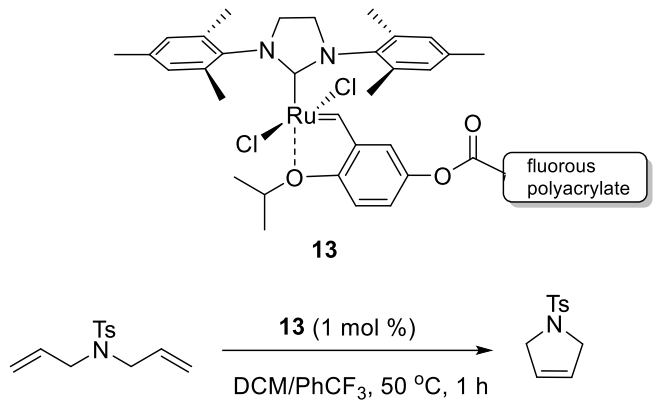
Scheme 12. Hydroformylation of 1-dodecene using a TMS of DMF and decane.

A fluorous biphasic system was also introduced by Horváth and Rábai in 1994 as a recyclable solvent system for the hydroformylation of 1-decene.[33] Fluorous biphasic systems involve the use of both a fluorous and a non-fluorous phase that are immiscible or that are temperature-dependent and may become one phase depending on the reaction conditions. Fluorous solvents are a good choice for use in a biphasic system because they have low solubility in water and in common organic solvents such as toluene, THF, and

alcohols. This insolubility allows for the products to be easily separated in the organic or aqueous phase while a catalyst containing fluorine groups can be recovered in the fluorous solvent phase and potentially recycled. In this initial report, Horváth and Rábai introduced a fluorous biphasic system of toluene and an analogous fluorous solvent where all of the hydrogens in toluene were replaced by fluorine. These solvents along with a fluorinated trialkylphosphine ligand and (acetylacetonato)dicarbonylrhodium(I) were used for the hydroformylation reaction of 1-decene with carbon monoxide and hydrogen at 100 ^{o}C. After the reaction was complete, the fluorous phase could be effectively separated from the product-containing toluene phase. Many examples have reported the use of fluorous biphasic systems or fluorous-supported catalysts for catalytic transformations,[34] but only two others will be described here.

In 2004, Yao reported a fluorous acrylate-supported Grubbs catalyst that was used for ring-closing metathesis reactions of a variety of dienes.[35] This catalyst **13** shown in Scheme 13 was prepared by copolymerization of a fluorous acrylate with acryloyl chloride followed by functionalization with 4-isopropoxy-3-vinylphenol and reaction of the functionalized copolymer with Grubbs 2nd generation catalyst and copper chloride. Catalyst **13** (1 mol %) was then used for ring-closing metathesis reactions with DCM and trifluorotoluene as solvents at 50 ^{o}C as shown in Scheme 13. When *N,N*-diallyl-4-methylbenzenesulfonamide was used as the substrate, the ring-closing metathesis reaction could be repeated for 15 cycles with an average ^{1}H NMR conversion of >98% to the cyclic product. Up to 20 cycles could be completed with a similar conversion, but the reaction time was increased to 2 h for cycles 15-20. The catalyst was cleanly recovered

after each cycle by removal of the solvent, addition of ethyl acetate, and extraction in FC-72, a fluorous solvent. The FC-72 solvent could also be recycled.

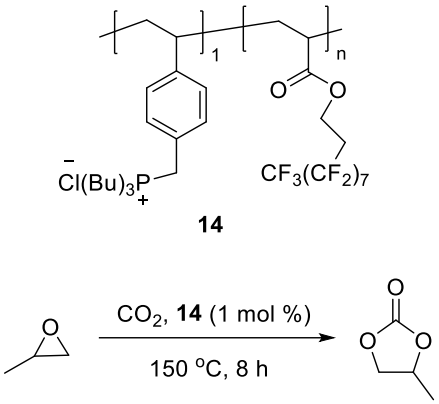


Scheme 13. Fluorous acrylate-supported catalyst **13** used for ring-closing metathesis reactions in a fluorous system.

More recently, Sakakura reported the use of a phosphonium chloride salt immobilized on a fluorous polymer as a catalyst for the synthesis of cyclic carbonates from epoxides and carbon dioxide.[36] This fluorous polymer-supported phosphonium salt **14** was prepared by the copolymerization of 4-vinylbenzyl chloride with a fluorinated polyacrylate followed by functionalization of the benzyl chloride groups with a tributylphosphonium chloride salt and is shown in Scheme 14. Catalyst **14** (1 mol %) was then used for the synthesis of propylene carbonate from propylene oxide and supercritical carbon dioxide ($scCO_2$) as the solvent. Surprisingly, this catalyst exhibited even higher activity than the low molecular weight phosphonium chloride salt after reaction at 150 ^{o}C

for 8 h (98% vs. 90% GC yield). It is likely that the fluorous side chain of the polymer increases the solubility of the phosphonium salt in $scCO_2$.

Catalyst **14** was also used to prepare a variety of cyclic carbonates with >88% isolated yields after 8 h. It was easily recycled in the reaction of propylene oxide with carbon dioxide. While a single phase formed initially at 150 ^oC with $scCO_2$ as a solvent, another phase of propylene carbonate formed during the reaction. After cooling to room temperature, the catalyst was precipitated by venting with carbon dioxide and was recovered by a simple filtration. It could be used for seven cycles giving an average product yield of >90% and after filtration, the product was isolated without the need for additional purification.



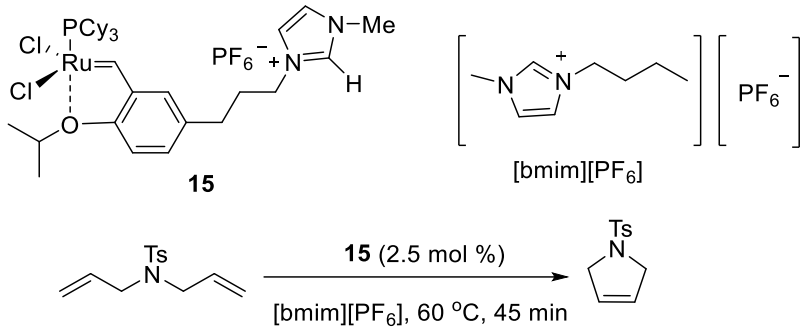
Scheme 14. Fluorous acrylate-supported phosphonium chloride salt **14** used for the synthesis of cyclic carbonates.

While solvent separation techniques such as aqueous biphasic systems and fluorous solvent extractions have the advantage of facile separation of the catalyst from the products after a catalytic reaction, they also have some drawbacks. Aqueous biphasic

systems cannot be used with catalysts or reactions that are water sensitive or water-insoluble, and fluorous recycling systems require the synthesis of fluorous-tagged catalysts as well as fluorous solvents, which are expensive compared to the organic solvents typically used for catalytic reactions. Ionic liquids have been introduced as yet another green solvent alternative, and interest in these solvents has heightened in the last two decades.[37] Ionic liquids are comprised of organic cations such as alkylammonium and alkylimidazolium paired with anions such as hexafluorophosphate or tetrafluoroborate to give salts which have a melting temperature at or below 100 ^{o}C. Ionic liquids are advantageous because they are nonflammable, chemically stable, and nonvolatile, meaning they can be easily recycled. Their chemical properties can also be modified by adjusting the cation and anion, making a wide range of properties possible. Ionic liquids can also be tuned to recycle a phase selective catalyst, as some examples will detail here.

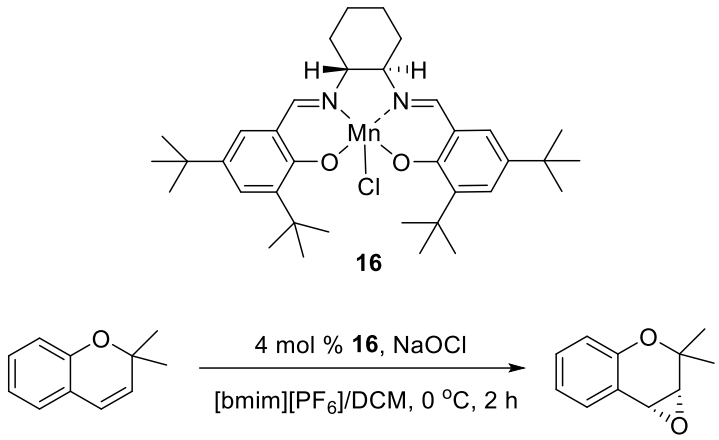
An example of an ionic liquid-supported catalyst for ring-closing metathesis reactions was reported by Mauduit and Guillemin.[38] This catalyst **15** shown in Scheme 15 was prepared by the reaction of 4-(dialkylimidazolium)-1-isopropoxy-2-vinylbenzene with Grubbs catalyst and copper chloride. Catalyst **15** was then used for ring-closing metathesis reactions of a variety of dienes in a 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) ionic liquid at 60 ^{o}C to give the corresponding cyclic products after 45 min. When *N*,*N*-diallyl-4-methylbenzenesulfonamide was used as the substrate, the cyclic product was obtained with >90% conversion for nine cycles, while the low molecular weight analogue of **15** gave only 40% conversion in the second cycle and 20% conversion in the third. The catalyst was easily recycled by extraction of the

product with toluene and reuse of the catalyst-containing ionic liquid by the addition of fresh substrate. It is interesting to note that the ninth cycle for the ring-closing reaction of *N*,*N*-diallyl-4-methylbenzenesulfonamide was accomplished after three months, meaning the ionic liquid could effectively store the generally air-sensitive Grubbs catalyst.



Scheme 15. Alkylimidazolium-functionalized Grubbs catalyst **15** used for ring-closing metathesis reactions in an ionic liquid.

Song also reported the use of an ionic liquid solvent system for epoxidation reactions using Jacobsen's chiral manganese(III) catalyst **16** shown in Scheme 16.[39] This catalyst (4 mol %) was effective for the asymmetric epoxidations of chromenes, indene, cis-β-methylstyrene, and 1-phenylcyclohexene in [bmim][PF_6]/DCM using sodium hypochlorite at 0 °C for 2 h. The products were obtained in >70% isolated yield and >84% enantiomeric excess (*ee*). While the epoxidation of 2,2-dimethylchromene could be completed in 2 h in the ionic liquid and DCM, when the ionic liquid solvent was removed in a control experiment the reaction required 6 h for completion, suggesting that the use of an ionic liquid enhances the reaction rate.



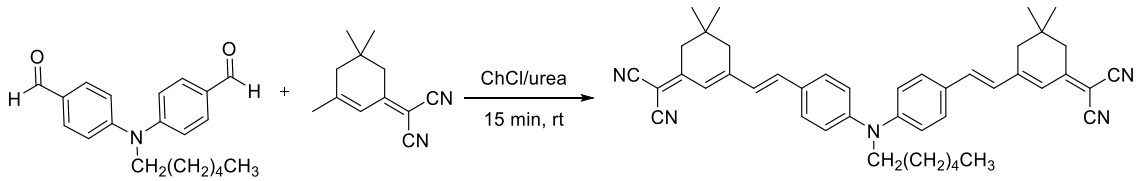
Scheme 16. Salen manganese(III) catalyst **16** used for asymmetric epoxidation in an ionic liquid.

Catalyst **16** was also recyclable in the ionic liquid/DCM solvent system for five cycles, giving an average isolated product yield of 69% with a gradual decrease in yield for each cycle from 86% in cycle 1 to 53% in cycle 5. The *ee* was consistent for the five cycles, only decreasing from 96% in cycle 1 to 88% in cycle 5. Recycling experiments were accomplished by washing the reaction solvent with water and then extracting the product from water using hexanes. The aqueous phase containing the ionic liquid and catalyst was then reused in subsequent cycles.

While ionic liquids have been gaining traction for many years as an alternative solvent, the study of deep eutectic solvents has also become of interest in recent years.[40] Deep eutectic solvents (DES), like ionic liquids, have two components, generally a quaternary ammonium salt such as choline chloride and a hydrogen bond donor such as glycerol or urea. When combined in certain ratios, a eutectic mixture forms with a substantially lower melting point compared to that of the individual components. DES

have the same advantages as ionic liquids including nonflammability and nonvolatility, but can be simpler to prepare and are often derived from inexpensive and nontoxic compounds with choline chloride/urea (ChCl/urea) being one well-known example.

In 2011, Shankarling reported the use of a ChCl/urea DES as a solvent system for Knoevenagel condensations to form styryl chromophores as shown in Scheme 17.[41] In this work, a variety of substrates were tested using a conventional procedure with piperidine and ethanol at reflux as well as a ChCl/urea DES solvent system. For the reaction of 4,4'-hexyliminobisbenzaldehyde with the isophorone-based active methylene compound shown in Scheme 17, the conventional procedure gave the corresponding product in 85% isolated yield after 4 h. In comparison, using the DES without any added base gave the condensation product in 95% yield after only 15 min. Other substrates supported this finding and showed that reactions carried out in the DES were much faster and the resulting product was obtained in higher yield compared with use of the traditional method.



Scheme 17. Synthesis of diphenylamine-based colorants by Knoevenagel condensation in a ChCl/urea DES.

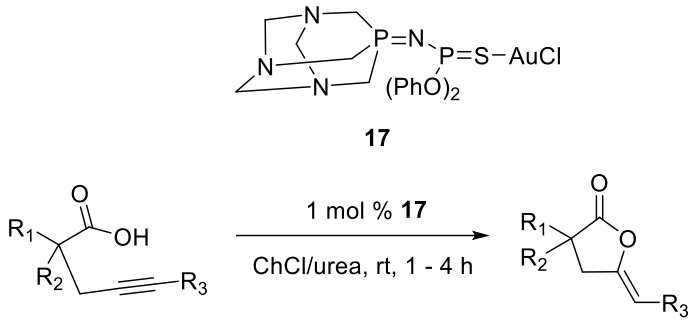
The DES solvent system was also recyclable. The reaction shown in Scheme 17 was carried out for six cycles with an average isolated product yield of 89%, although the

yield dropped noticeably in the last two cycles. Recycling was easily accomplished by adding water to precipitate the product followed by reuse of the DES by the addition of fresh substrate. A later report by Xu suggested the same ChCl/urea DES could be used in a catalytic amount (20 mol %) for the Knoevenagel condensation reactions of substituted benzaldehydes with activated methylene compounds.[42] Recycling of the DES in this case was also possible to give the product of the condensation reaction between benzaldehyde and ethyl cyanoacetate in 86% average yield after 2 h for five cycles.

In 2014, García-Álvarez reported the use of a ChCl/DES for the cycloisomerization of γ-alkynoic acids using the iminophosphorane-gold(I) complex **17**.[43] Catalyst **17** was prepared by the reaction of a 1,3,5-triaza-7-phosphaadamantane-based iminophosphorane ligand with chloro(dimethylsulfide)gold(I) and is shown in Scheme 18. Catalyst **17** (1 mol %) was first tested in the cycloisomerization reaction of 4-pentynoic acid in a variety of DES. Typically, this reaction requires the use of a base, but because certain DES are known to exhibit basic character (such as ChCl/urea), no additional base was utilized for these reactions. Using ChCl/urea, ChCl/glycerol, and ChCl/ethylene glycol as solvents gave the cycloisomerization product in 99% isolated yield, but as ChCl/urea gave the product after only 15 min, it was utilized in further reactions. It is interesting to note that the product was obtained more quickly in ChCl/urea than in other green solvents such as water and glycerol or organic solvents such as toluene.

When 2-(ethoxycarbonyl)-2-methylpent-4-ynoic acid was used as the substrate for cycloisomerization, the catalyst could also be reused in ChCl/urea for three additional cycles, although cycles 3 and 4 required an additional hour of reaction time to obtain the

same GC yield (>90%). The product was easily recovered from the DES after the reaction by extraction with diethyl ether and the DES phase was then reused by the addition of fresh substrate.

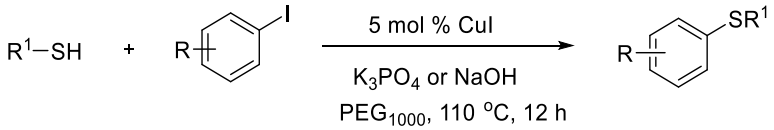


Scheme 18. Cycloisomerization reactions of γ-alkynoic acids using the iminophosphorane-Au complex **17** as a catalyst in a ChCl/urea DES.

While not as commonly utilized as some of the other alternative solvents mentioned, examples of the use of polymers as solvents or cosolvents have also emerged in recent years. These solvents have many of the same advantages as ionic liquids and DES such as low volatility, low flammability, and recyclability. They are also generally nontoxic. PEG is perhaps the most commonly utilized polymer solvent.[44] In 2004, Wang reported the deprotection of 1,1-diacetates using PEG of molecular weight 400 Da (PEG_{400}) as a solvent.[45] Commercially available indium(III) bromide was used as the catalyst (10 mol %) in PEG_{400} at 80 ^{o}C to deprotect a variety of aromatic 1,1-diacetates to give the resulting aldehydes in >90% isolated yield. Short reaction times (within 1 h) were required for most substrates with the exception of aromatic nitro compounds which required 3 h to give comparable yields. When phenylmethylene diacetate was used as the

substrate, the catalyst could be reused for four cycles with an average product yield of 95%. Catalyst recycling was accomplished simply by extracting the product with diethyl ether and adding fresh substrate to the PEG phase.

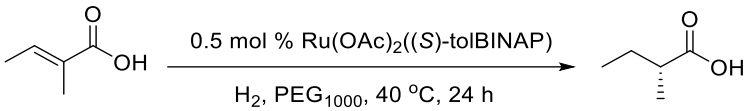
Wang also reported the use of PEG_{1000} as a solvent for C-S couplings of aryl iodides and thiols as shown in Scheme 19.[46] When 5 mol % of copper iodide was used with potassium phosphate in PEG_{1000}, coupling reactions of aryl iodides and aromatic thiols were carried out using both electron-rich and electron-deficient aryl iodides to give the products in high yield (>85% after 12 h at 110 ^{o}C). When iodobenzene and benzenethiol were used as substrates and sodium hydroxide was used as the base, the copper iodide catalyst could be recycled in PEG and the resulting products were obtained with an average isolated yield of 97% for six cycles. After each cycle, the products were extracted with petroleum ether and the catalyst-containing PEG phase was reused without any additional treatment.



Scheme 19. Copper-catalyzed C-S cross-coupling reactions in PEG.

In 2006, Jessop also reported the asymmetric hydrogenation of tiglic acid using PEG_{1000} as a solvent.[47] This reaction, shown in Scheme 20, was accomplished by the use of 0.5 mol % BINAP-ruthenium(II) catalyst and hydrogen in PEG_{1000} at 40 ^{o}C for 24 h. A 94% average GC yield and 83% average *ee* were obtained for five cycles. After the

reaction was complete, the product was extracted from the PEG solvent using $scCO_2$ and then the catalyst was recycled by the addition of fresh substrate. Unlike many other examples using PEG, this example used a green solvent to isolate the products.

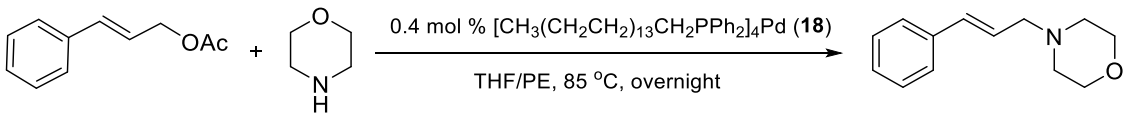


Scheme 20. Asymmetric hydrogenation of tiglic acid using a ruthenium-incorporated BINAP catalyst in PEG.

The Bergbreiter group has reported several examples of using nonpolar polymers as solvents or cosolvents in recent years.[20,48] In general, this work focused on relatively low molecular weight PE oligomers that are commercially available with low Đ.[49] As previously described, using nonpolar solvents versus polar solvents to recycle phase selective catalysts has the added advantage of increased substrate versatility for the catalytic reactions being tested. In 2012, Bergbreiter reported the use of a THF/PE_{400} solvent system for allylic amination reactions using the PE-supported tetrakis(triphenylphosphine)Pd(0) analogue shown in Scheme 21.[48] This PE-supported diphenylphosphine palladium catalyst **18** was prepared by the reaction of a mesylate-terminated PE with potassium diphenylphosphide and then palladation with tris(dibenzylideneacetone)dipalladium(0).

Catalyst **18** (0.4 mol %) was then used in the allylic amination of cinnamyl acetate with morpholine using THF/PE as the solvent system at 85 °C. The ca. 1:3 mixture of THF and PE was immiscible at room temperature but formed one phase upon heating. After the

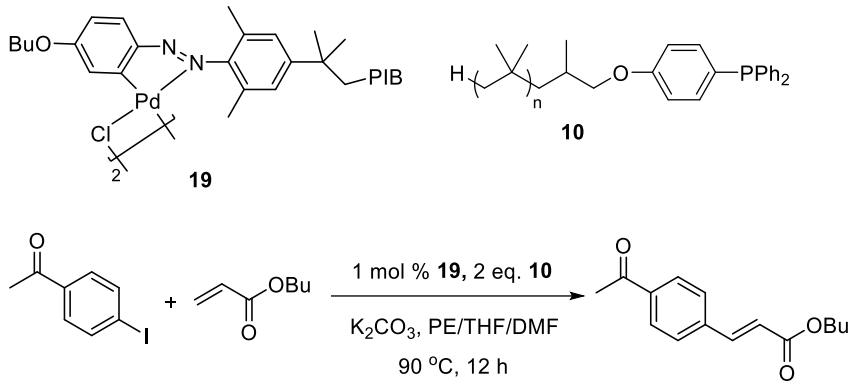
reaction, the solvent could be perturbed by the addition of water to give a viscous PE phase and an aqueous THF phase. The reaction was then cooled and the product-containing THF phase was removed. The catalyst could then be recycled by the addition of fresh substrates in THF to the PE wax containing the catalyst. The catalyst-containing PE wax was recycled four times, giving an average isolated product yield of 83%. Leaching of palladium metal into the THF product-containing phase was also low (0.2%) in the third and fourth cycle. This result is consistent with the previously reported example where the use of PE as a cosolvent was able to substantially reduce the amount of metal leaching.[20]



Scheme 21. PE-supported **18** as an analogue of tetrakis(triphenylphosphine)Pd(0) for use in allylic amination reactions in a PE/THF solvent system.

In 2013, the Bergbreiter group reported another example of a solvent system where PE_{400} was used as a cosolvent with THF and DMF for Heck reactions of aryl halides using the PIB-supported azobenzene palladium(II) catalyst **19**.[50] Catalyst **19**, shown in Scheme 22, was synthesized by the reaction of a PIB-supported phenol azo dye with butyl bromide followed by palladation with bis(benzonitrile)palladium(II) chloride. It was then examined as a catalyst (1 mol %) for the Heck reaction of 4'-iodoacetophenone and butyl acrylate in a ca. 1:1:1 solvent system of PE/THF/DMF at 90 °C for 12 h. The product was obtained in high yield and the catalyst could be recycled by the addition of hot water to perturb the two phases followed by cooling to room temperature to separate the catalyst-

containing PE phase from the THF/DMF phase containing the product. After the polar phase was removed, the catalyst-containing PE wax could be recycled by the addition of fresh THF/DMF and substrates. A 90% average isolated product yield was obtained for the five cycles, and 1.2% metal leaching into the product was determined by ICP-MS in cycle 4.



Scheme 22. PIB-supported dye-based palladium catalyst **19** and phosphine ligand **10** used in Heck reactions in a PE/THF/DMF solvent system.

This lower level of leaching is in stark contrast to what was seen with heptane/DMF as a solvent system for the same reaction. Using heptane/DMF gave the product in similar yield after recycling (a 92% average yield was obtained for 5 cycles) but showed leaching of ca. 7% of the metal into the product after the fourth cycle. This is yet another result that suggests that not only is PE a green and recyclable solvent, but it also can reduce leaching of precious metals or catalysts into the product-containing polar phase. Furthermore, addition of the PIB-supported triphenylphosphine ligand **10** to the same Heck reaction using a PE/THF/DMF system gave similar product yields (89% after

5 cycles) and the catalyst and ligand were recycled using the same method previously described. However, the addition of **10** lowered the palladium leaching even more markedly from the 1.2% value observed for the typical PE/THF/DMF system to only 0.12%.

As illustrated by these examples, the use of hydrocarbon polymer solvents is a viable alternative to the use of more toxic organic solvents. These polymers, usually in the form of relatively low molecular weight oligomers, can serve either as solvents or cosolvents. They can also reduce leaching of precious metals or catalysts into the product phase of a catalytic solvent system. Most importantly, they do not leach appreciably themselves into the product phase. In the next chapter, the use of nonpolar hydrocarbon oligomer solvents other than PE will be discussed.[51,52] This discussion includes the use of both PIB and poly(α-olefins) (PAOs) as solvents or cosolvents. The results show that these materials, like the PE oligomer cosolvents or solvents discussed above, lower leaching of polymer-supported materials into a polar phase.

CHAPTER II

SYNTHESES OF PIB-SUPPORTED AZO DYES AND STUDIES OF THEIR USE AS CATALYST SURROGATES TO STUDY ALTERNATIVE THERMOMORPHIC SOLVENT SYSTEMS[*]

Introduction

Solvents are a ubiquitous part of many if not most chemical processes. They serve useful roles in mitigating exotherms, in providing a suitable milieu for reactions, and in controlling relative concentrations of reacting species. They are essentially required in homogeneous catalysis. However, solvents pose environmental issues and introduce additional costs in any system. Ideally, they should be easily recyclable by a simple physical process. In practice, they often have to be recovered by energy intensive processes like distillation. If they are not recovered, they are disposed of as chemical waste. Lists of greener and more environmentally benign solvents that include new types of solvents as well as more benign and more sustainable organic solvents exist.[53,54] However, it is difficult if not impossible to design solvents that have all the desired criteria

[*] Reprinted with permission from "Using Soluble Polymers to Enforce Catalyst-Phase-Selective Solubility and as Antileaching Agents to Facilitate Homogeneous Catalysis" by Liang, Y.; Harrell, M. L.; Bergbreiter, D. E. *Angew. Chem. Int. Ed.* **2014**, *53*, 8084-8087, Copyright 2014 by WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim and with permission from "Alternatives for Conventional Alkane Solvents" by Harrell, M. L.; Malinski, T.; Torres-López, C.; Gonzalez, K.; Suriboot, J.; Bergbreiter, D. E. *J. Am. Chem. Soc.* **2016**, *138*, 14650-14657, Copyright 2016 by American Chemical Society.

for a green solvent.[55] For example, sustainable bioderived organic solvents are often still volatile and as such can introduce unwanted pollutants into the environment.

This chapter describes studies of oligomeric hydrocarbons that can serve as substitutes for conventional alkane hydrocarbon solvents. These alternative solvents are greener than typical hydrocarbon solvents such as hexane or heptane. As solvents, they are as good as or as bad as these conventional alkane solvents. They readily dissolve alkane-soluble species and behave as nonsolvents toward polar substrates. However, oligomeric hydrocarbon solvents have some significant advantages over their low molecular weight alkane analogues. First, they are nonvolatile and relatively nontoxic.[56–58] Second, unlike lower molecular weight alkanes, they do not significantly contaminate polar phases when used in conjunction with polar solvents. This is true when the nonpolar and polar solvents are separated by a liquid/liquid separation after heating an initial biphasic mixture to form a single phase and then cooling to reform the biphasic mixture, a thermomorphic process.[15]

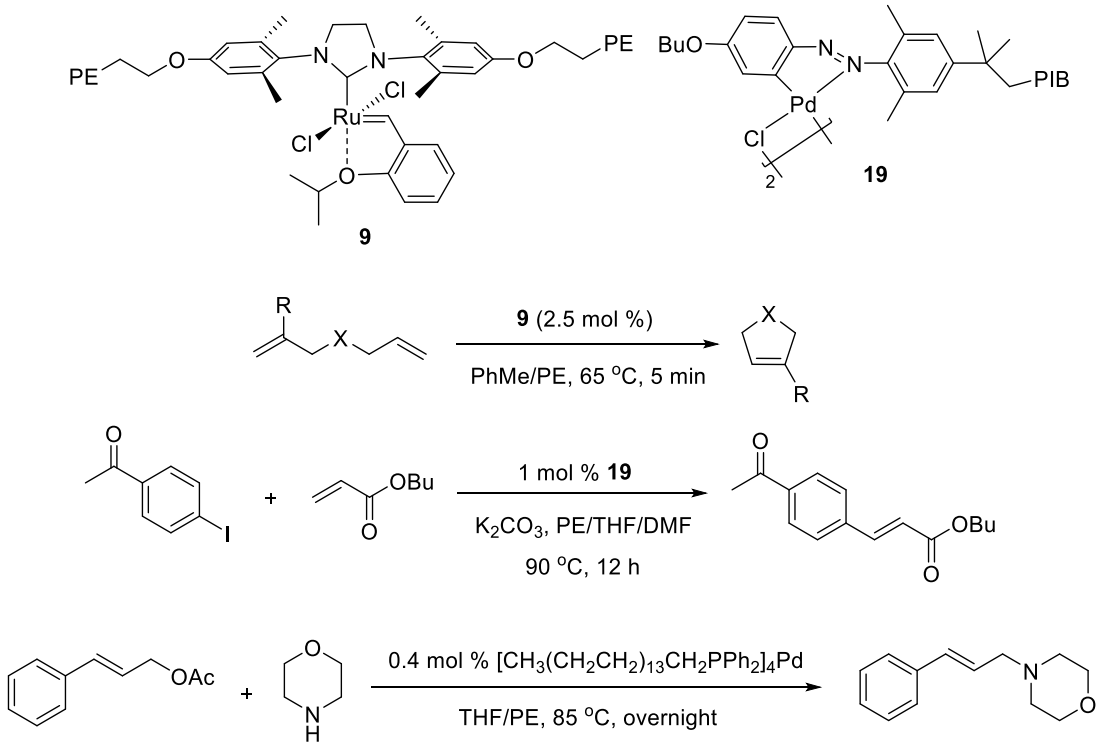
Recent work in our group has focused on designing soluble polymer-bound catalysts that can be used in a fully miscible solvent mixture yet can be separated in a biphasic separation step after a homogeneous catalytic reaction.[59] This work uses inexpensive oligomeric phase tags derived from heptane-soluble oligomers or polymers. With such phase tags, it is possible to effect a biphasic recovery of reagents or catalysts that have high alkane phase selective solubility if they have a stable resting state or to separate catalyst and ligand residues from polar phase soluble products.[26,60] A disadvantage of these procedures is that they use alkanes like heptane as the nonpolar

phase. While most of this solvent can be recovered and reused, it has some undesirable characteristics due to its volatility. Moreover, a portion of it cannot be readily recovered because it partitions into the polar phase and is lost.

Some of this prior work suggested that hydrocarbon oligomers could be a sustainable alternative to a conventional alkane solvent like heptane. One example was the observation that a commercially available low melting point polyethylene (PE) wax[49] could recover catalysts in a nonvolatile and nontoxic solid paraffin-like matrix that can both protect a catalyst from adventitious decomposition by polar reagents and effect a simple filtration based separation.[21,61,62] Our group subsequently showed that these PE waxes can be used as cosolvents to reduce metal leaching and leaching of homogeneous polymer-supported catalysts.[48,50] Some examples of catalytic reactions from our group that have used PE as a cosolvent are shown in Scheme 23.

In this chapter studies of polypropylene (PP) oligomers, PIB oligomers, and readily available poly(α-olefin)s (PAOs) are detailed where these oligomers are used as solvents and cosolvents. Chronologically these studies followed initial studies using a PIB-bound Rh(II) catalyst that showed that the use of such nonpolar phase soluble oligomeric cosolvents helped prevent undesired side reactions. These earlier studies also showed that oligomeric cosolvents were able to reduce the leaching of an azo dye and a metal complex into the polar phase of a thermomorphic system. These observations were then expanded in further studies of this "anti-leaching" effect that were carried out using PIB-bound azo dyes as catalyst surrogates. Those subsequent studies investigated the properties of thermomorphic systems where nonpolar phase soluble oligomers were used

as solvents or cosolvents and showed that such inexpensive polyolefin oligomers can indeed serve as a replacement for heptane. Those subsequent studies not only showed that these oligomers are as functional as heptane as solvents, but also that they do not appreciably leach into a polar phase. A reduction in leaching of the polymer-supported azo dye catalyst surrogates into the polar phase was also observed when these oligomeric solvents were used. Finally, further studies of both thermal and acid-promoted dye isomerization by a coworker showed that reactions in these oligomeric solvents mirror reactions in heptane.



Scheme 23. Catalytic reactions carried out using a PE wax as a cosolvent.

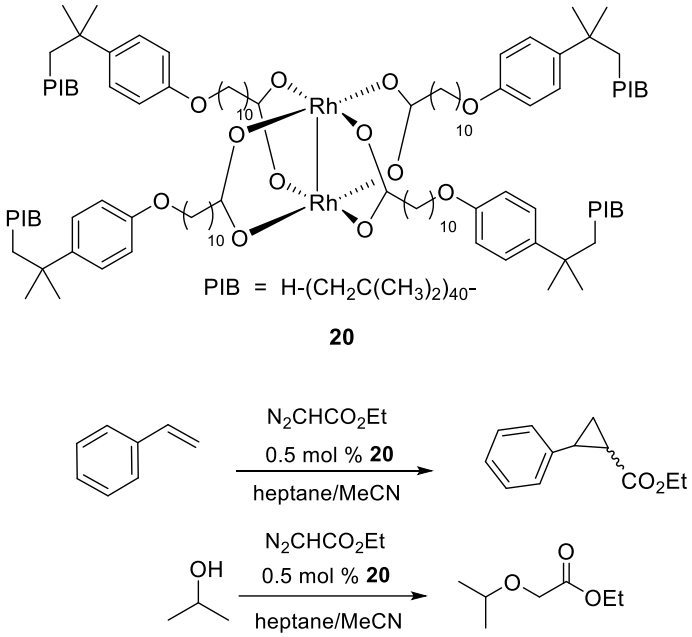
Results and Discussion

One of the first studies that heightened interest in using a nonpolar oligomer solvent or cosolvent other than PE was done by a coworker, Dr. Yannan Liang, and involved the use of the PIB-supported Rh(II) catalyst **20** for cyclopropanation and O-H insertion reactions. While this catalyst had been previously prepared by our group and was recyclable, it required the use of a syringe pump to add the ethyl diazoacetate (N_2CHCO_2Et) reagent to minimize the facile and exothermic dimer formation.[63] Therefore, it was advantageous to create a system where syringe pump addition was not needed.

To accomplish this goal, a biphasic mixture of heptane and MeCN was tested as a solvent system for these cyclopropanation and O-H insertion reactions (cf. Scheme 24). This solvent mixture was chosen based on the idea that heptane and MeCN are immiscible. Since N_2CHCO_2Et is relatively insoluble in heptane versus MeCN and since catalyst **20** has high phase selective solubility in heptane, it was hypothesized that the phase separation of N_2CHCO_2Et and **20** would lower the rate of dimer formation if the rate of dimer formation were second order in N_2CHCO_2Et. Cyclopropanation rates would also be decreased using this solvent mixture, but less so because styrene, one of the reactants in the cyclopropanation, readily dissolves in the heptane phase containing **20**.

These studies confirmed that the use of the heptane/MeCN biphasic system was able to minimize dimer formation similarly to using syringe pump addition. However, adding unfunctionalized PIB was able to reduce the dimer formation even further. This

suggested that polymer cosolvents can be used not only to minimize catalyst leaching, but also as an aid to help prevent unwanted side reactions.



Scheme 24. Cyclopropanation and O-H insertion reactions using PIB-supported Rh(II) catalyst **20**.

In this work, there were two possible explanations for the dimer formation. The dimer either resulted from minimal catalyst **20** leaching into the N_2CHCO_2Et-rich MeCN phase, from an increased N_2CHCO_2Et concentration in the heptane phase, or from a combination of these scenarios. Thus, this byproduct formation could be lowered by reducing the leaching of **20** into MeCN or by further reducing the concentration of N_2CHCO_2Et in the heptane phase. The studies mentioned addressed this problem by the

addition of unfunctionalized PIB to the heptane phase, based on the notion that added PIB might decrease leaching of **20**. The premise was that addition of unfunctionalized PIB would competitively saturate the MeCN phase, reducing the amount of **20** in that phase. However, the result of lower dimer formation by addition of unfunctionalized PIB to the heptane phase did not prove that the leaching of **20** into the MeCN phase was decreased. Because there was no visually apparent leaching of **20** into the MeCN phase, this idea had to be studied using chromogenic surrogates for **20**. In this case, this issue was investigated by examining how added hydrocarbon polymer cosolvents reduced the leaching of two chromogenic PIB derivatives **11** and **21** shown in Figure 5.

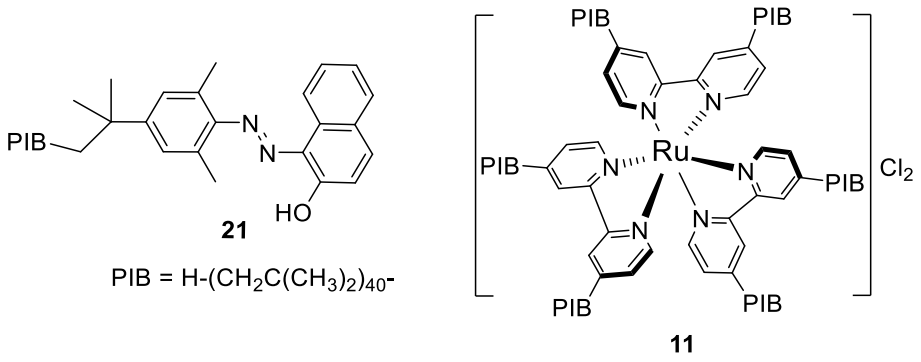


Figure 5. PIB-supported azo dye **21** and PIB-supported ruthenium bypyridine complex **11** used in leaching studies with oligomer cosolvents.

The first study of the anti-leaching effect of added hydrocarbon cosolvents used the PIB_{2300}-bound azo dye **21** synthesized by a known procedure[64] in a thermomorphic mixture containing 3 g of heptane and 3 g of methanol. In this system, **21** had a small but detectable solubility in methanol at 25 ^{o}C with an absorbance of 0.36 at 492 nm by UV-

Visible spectroscopy. Replacing 1 g of the heptane with 1 g of a PP oligomer[65] decreased the leaching of **21** by ca. 30%, giving an absorbance of 0.25 in methanol. When 3 g of PP and 3 g of methanol were used as the solvent mixture, the concentration of **21** in the methanol phase dropped by over 50%, giving a methanol absorbance of 0.16. This reduction in leaching seen in the PP/methanol system versus a heptane/methanol system is shown in Figure 6.

Figure 6. Leaching of the PIB-supported azo dye **21** into the methanol phase in either heptane/methanol (left) or PP/methanol (right) solvent systems. Reprinted with permission from (*51*).

Another study with a chromogenic PIB-bound ruthenium bipyridine complex **11** used previously as a photoredox catalyst[26] conducted by Dr. Yannan Liang showed an anti-leaching effect of added hydrocarbon polymer as well. When **11** was dissolved in a thermomorphic heptane/ethanol/DMF (4/2/3 vol/vol/vol) system, a monophasic solution formed at 90 ^{o}C that became biphasic on cooling to 25 ^{o}C. Reheating and adding 0.4 g of

PIB_{2300} to the hot monophasic system followed by cooling to reform a biphasic mixture at 25 ^{o}C drastically decreased the leaching of **11** into the polar phase as shown in Figure 7.

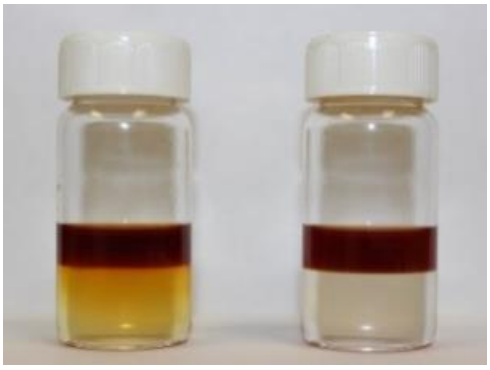


Figure 7. Anti-leaching effect of PIB_{2300} for the ruthenium bypyridine complex **11** in a heptane/ethanol/DMF solvent system; no PIB (left) or 0.45 g of added PIB_{2300} in 4 mL of a heptane phase containing 80 mg of **11** (right). Reprinted with permission from (*51*).

This work showed the potential of an oligomeric hydrocarbon cosolvent such as PIB to help prevent unwanted side reactions such as dimerization. While the oligomer cosolvent may have also prevented minor catalyst leaching into MeCN, its main advantage was its ability to effectively segregate the phases and to lower the concentration of N_2CHCO_2Et in the nonpolar heptane phase containing the PIB-supported Rh(II) catalyst. However, studies with the chromophores **11** and **21** that showed a reduction in leaching of the PIB-supported dye or metal complex into the polar "product" phase when oligomeric cosolvents were used are also important results that can be applied to catalysis where a catalyst's effectiveness in recycling schemes is compromised by its leaching into the product phase. Use of such anti-leaching solvents could also simplify purification of the product formed in a catalytic reaction if metal or ligand leaching into the product were

lowered. For these and other reasons, we pursued further studies with oligomeric hydrocarbon solvents to see if they could generally affect leaching of catalysts or catalyst surrogates and to determine if such solvents could truly serve as a replacement for heptane.

The main focus of our following studies with alternative solvents is a particular class of oligomeric hydrocarbons, poly(α-olefin)s (PAOs), which are prepared on a large scale from 1-alkenes and are most often used as lubricants.[66] These syntheses of PAOs are carried out using acid- or transition metal-catalyzed oligomerization reactions. Complex mixtures of constitutional isomers form, even in a dimerization.[67] Nonetheless, various PAOs with characteristic viscosities, average molecular weights and boiling points, and modest dispersity are inexpensive and commercially available.[68,69] Conventional alkanes like hexane and heptane have inhalation toxicity.[70,71] Hexane in particular is not recommended as a solvent due to its volatility and neurotoxicity.[70] PAOs in contrast are nonvolatile and do not have inhalation toxicity due to their low vapor pressure. They also have low oral toxicity.[58]

However, like all alternative solvents, PAOs have some potential disadvantages too. For example, their lack of bioavailability, especially for the larger PAOs used in these studies, limits their biodegradability.[69,72] While lower molecular weight PAOs are biodegradable, the higher molecular weight PAOs degrade more slowly and could accumulate in the environment though they reportedly do not bioaccumulate in aquatic organisms.[69] The viscosity of PAOs is also an issue. All PAOs are more viscous than conventional alkanes like hexane or heptane and most conventional solvents. The viscosity of what we suggest as a preferred PAO solvent in the following work is 10 cSt at 100 °C,

a viscosity like that of olive oil at 95 °C (9.5 cSt).[73] PAOs are also flammable. However, the flash point of PAOs is >150 °C while heptane has a flash point of −4 °C.[68] Finally, PAOs without the addition of another cosolvent are simply alkanes. Thus, PAOs will not be any better than hexane or heptane as pure solvents for even modestly polar organic molecules.

Our initial studies focused on three PAOs (PAO_{687}, PAO_{1758}, and PAO_{2505}) that we obtained from Exxon Mobil.[68] Similar PAOs are available from other sources.[69] These PAOs were chosen because we hypothesized that materials with these molecular weights would be more easily separable from polar solvents. We also believed that higher molecular weight PAOs would be better anti-leaching agents because they more closely resemble PIB with M_n values of 1000 or 2300 Da. However, these inexpensive, commercially available compounds come in a variety of molecular weights varying from M_n values of 280 to 4150 Da with dispersity values that range from 1.12 to 1.82 Đ (cf. Table 1). These materials have a range of viscosities that vary from 2 to 150 cSt at 100 °C. These viscosities increase upon cooling, but here we report the 100 °C viscosity values as they are most relevant to processes that might involve heated thermomorphic solvent mixtures. The viscosity of olive oil is comparable to that of PAO_{687} at ca. 100 °C. Depending on the specific PAO and whether the PAO is used with or without a cosolvent, viscosities of some PAOs as pure solvents or most PAO-cosolvent mixtures are manageable.

PAO_{687}, PAO_{1758}, and PAO_{2505} were used in the following studies. PAO_{2505} has too high a viscosity to make it a useful solvent for ambient temperature reactions. However,

it could be useful as a cosolvent. PAO_{687} has a viscosity similar to that of olive oil. PAO_{1758} has an intermediate viscosity. All of these PAOs are colorless liquids. They are all fully hydrogenated, and in ^{1}H NMR spectroscopy, their signals all occur between δ 0.8 and 1.4.

Table 1. Properties of poly(α-olefin) (PAO) alternative solvents.[a]

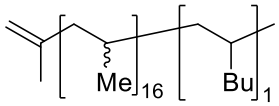
PAO (M_n)	Approximate Number of Carbons	Dispersity Index	Viscosity at 100 ^{0}C (cSt)	Density (g/mL)
PAO_{283}	20	--	2	--
PAO_{432}	31	--	4	--
PAO_{570}	41	--	6	--
PAO_{611}	44	1.12	8	--
PAO_{687}	49	1.12	10	0.84
PAO_{1758}	125	1.35	40	0.85
PAO_{2505}	179	1.47	65	0.85
PAO_{2939}	210	1.82	100	--
PAO_{4146}	296	1.69	150	--

[a]Dispersity and M_n data were supplied by Dr. Wenning Han from Exxon Mobil. Other data including viscosity and density data are available from online resources.[68]

These studies also included two other polyolefin oligomers as solvents or cosolvents. One example is a propylene-hexene random copolymer that is like a catalyst support others have used.[65] This polymer **22** shown in Figure 8 contains alkene end groups derived from either propylene or hexene units.[74] **22** was obtained as an 800 Da material from Baker-Hughes. It has a 25 °C viscosity that is qualitatively similar to that of PAO_{687}. It is not commercially available so its use in our studies was limited. PIB with a terminal double bond and in a hydrogenated form is available too. While we have used PIB as a ligand and while PIB derivatives are commercially available, nonvolatile, and nontoxic,[75]

vinyl-terminated PIB with molecular weights of 1000 and 2300 Da have viscosities of 190 and 1500 cSt at 100 °C, viscosities that are too high for PIB to be used as a pure solvent.

We first examined the use of PAO_{687}, PAO_{1758}, PAO_{2505}, **22**, and PIB_{1000} with other cosolvents (Table 2). The PAOs, **22**, and PIB_{1000} were fully soluble in alkanes, toluene, DCM, and THF when a 1/1 (w/w) mixture of the PAO and solvent was prepared. A 1/1 (w/w) mixture of the PAO and methanol, ethanol, isopropanol, DMF, MeCN, and water formed biphasic mixtures at room temperature. The PAOs and **22** showed varying levels of thermomorphic behavior with alcohols with temperature dependent solubility behavior that was similar to that of heptane.



22

Figure 8. Polypropylene-hexene random copolymer **22** used in leaching studies.

As noted above, an initial concern was that hydrocarbon oligomers could contaminate a polar phase. This is a concern because if there were significant contamination, such hydrocarbon oligomer contaminants would have to be removed from products by extractions with alkanes or by chromatography. While such contaminants could be easily removed, such additional purification steps would be a significant liability for an alkane solvent substitute. We hoped to minimize this issue by choosing higher molecular weight PAOs as our initial candidates but this was nonetheless an issue that had

to be tested. To test this issue, a version of a ^{1}H NMR experiment that relies on the 1.1% natural abundance of ^{13}C was carried out. We have used this technique to assay end functionalized PEG M_n values,[76] and others have used it to analyze trace impurities in products in asymmetric synthesis.[77]

Table 2. Solubility of oligomeric alternative solvents with conventional solvents.

Solvent	Oligomer	Solubility
Heptane	PAOs, **22**, PIB	Yes[a]
Toluene	PAOs, **22**, PIB	Yes[a]
DCM	PAOs, **22**, PIB	Yes[a]
THF	PAOs, **22**, PIB	Yes[a]
Methanol	PAOs, **22**	Thermomorphic[b]
Ethanol	PAOs, **22**	Thermomorphic[b]
Isopropanol	PAOs, **22**	Thermomorphic[b]
DMF	PAOs, **22**	Thermomorphic[b]
MeCN	PAOs, **22**, PIB	No
Water	PAOs, **22**, PIB	No

[a]1 g of the PAO visually dissolved in 1 g of the low molecular weight solvent at room temperature. [b]1 g of the PAO mixed with 1 g of the low molecular weight solvent formed a homogeneous solution on heating to ca. 100 °C. Reprinted with permission from (*52*).

In an experiment done by Dr. Jakkrit Suriboot, a 10 mL solution of a 3:2:5 (w/w/w) thermomorphic mixture of cyclooctane, **22**, and DMF was examined. When this mixture was heated to ca. 70 °C, a monophasic solution formed. On cooling to room temperature, it again became biphasic. At that point, it was possible to isolate the DMF phase and to show by integrating the DMF peak at δ 8.0 versus the cyclooctane peak at δ 1.3 the amount of the cyclooctane that had partitioned into the denser DMF phase. In addition to the cyclooctane singlet at δ 1.3, two satellite peaks due to the 1.1% natural abundance of ^{13}C in cyclooctane appeared. When the ^{1}H NMR spectrum in the δ 0.5-2.0

region was carefully examined, the cyclooctane peak and the ^{13}C satellite peaks were the only signals seen. No peaks attributable to the oligomer **22** were seen. This corresponds to leaching of < 0.1% and to the presence of less than 100 ppm of **22** in the DMF phase. This level of contamination of **22** in the polar phase was judged to be insignificant.

This promising result of little contamination of the polar phase by **22** led us to quantitatively study the extent to which PAO_{687}, PAO_{1758}, and PAO_{2505} significantly contaminate a polar phase when used as solvents (cf. Table 3). To carry out these studies, we used a version of the ^{1}H NMR experiment previously described. In this case, we relied on the 1.1% natural abundance of ^{13}C in methanol, DMF, and MeCN and examined 6 g of a 1:1 (w/w) mixture of the PAO and methanol, DMF, or MeCN as the polar solvent. When the PAO and methanol or DMF were heated, these solvent mixtures exhibited thermomorphic character and a monophasic solution formed at 100 °C. On cooling to room temperature, these solutions became biphasic. The PAO/MeCN mixtures were always biphasic. They were heated with stirring for 24 h at ca. 100 °C. We believe this heating and stirring time was sufficient to reach phase equilibrium for the PAO and MeCN mixture, since experiments carried out for 48 h showed no significant change in the percent leaching of PAO_{687}, PAO_{1758}, and PAO_{2505} into MeCN.

After cooling the solvent mixtures to ambient temperature, the polar phase was isolated and the amount of the PAO present was determined by integrating the satellite of one of the polar solvent peaks and comparing it to the integration of the known PAO peak. We did not determine if cooling to room temperature lowered this level of contamination of the PAO in MeCN. However, since we believe that the solubility of PAO in MeCN

does not increase on cooling, the trace amounts of PAO in MeCN we measured are a maximum amount of contamination for this polar phase.

Table 3. ^{1}H NMR analysis of PAO leaching into the polar phase of a polar solvent/PAO solvent system.[a]

Oligomer	Polar Solvent	PAO in the polar phase (mg)[b]	PAO leaching (%)[c,d]
PAO_{687}	Methanol	1.0	0.03
PAO_{1758}	Methanol	0.4	0.01
PAO_{2505}	Methanol	0.5	0.02
PAO_{687}	DMF	0.3	0.01
PAO_{1758}	DMF	2.0	0.06
PAO_{1758}[e]	DMF	3.4	0.12
PAO_{2505}	DMF	24.0	0.80
PAO_{687}	MeCN	1.0	0.03
PAO_{1758}	MeCN	0.4	0.01
PAO_{2505}	MeCN	0.4	0.01

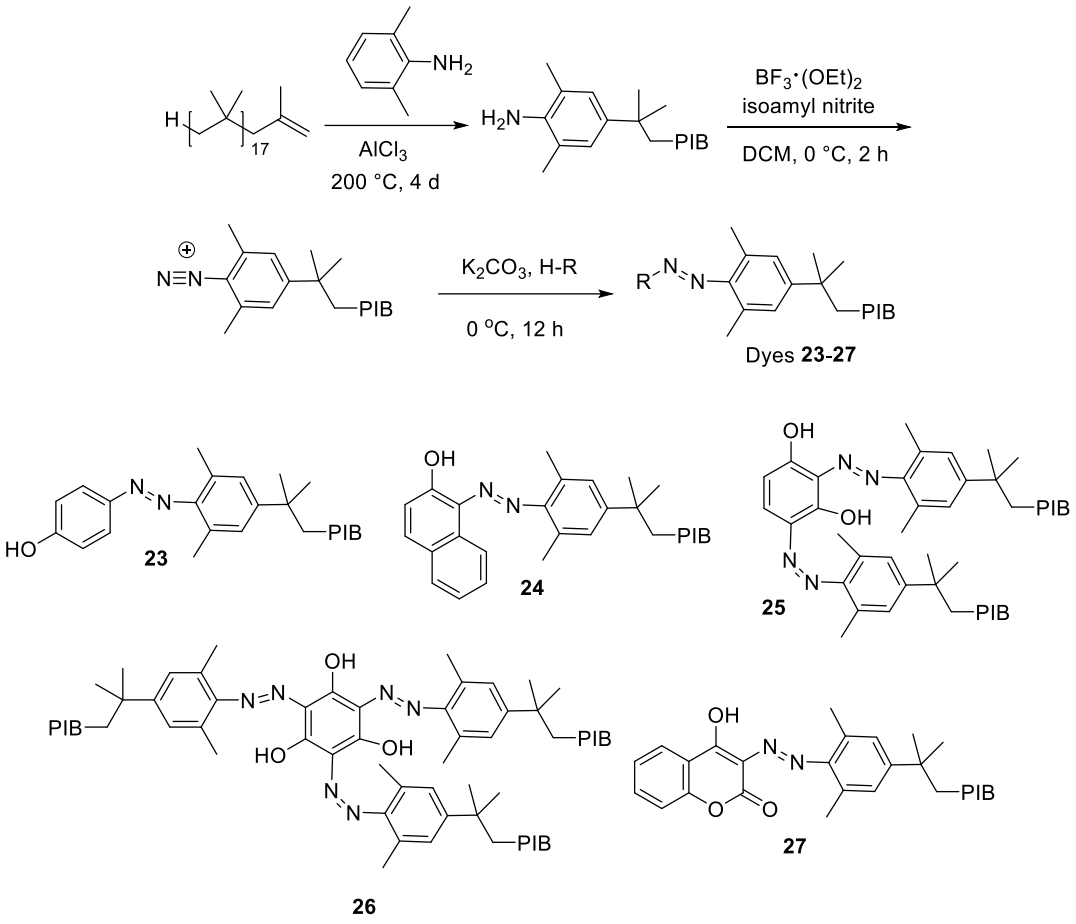
[a]A biphasic mixture of 3 g of the PAO and 3 g of the polar solvent was heated to form a single phase and then cooled to reform a biphasic mixture. Then a drop of the polar solvent solution was removed for ^{1}H NMR spectroscopic analysis using $CDCl_3$ as the solvent. These analyses were carried out at ambient temperature with the exception of the methanol samples which required analysis at -30 °C to shift the methanol -OH peak away from the PAO peak being analyzed. [b]The mg amount of the PAO in the polar phase was calculated by setting the integral for the formyl H of DMF or the methyl singlets of methanol or MeCN to 100 and comparing 1.08% of this integral to the integration of any detectable PAO peak between δ 0.8 and 1.4. [c]The percent leaching of the PAO was based on the mg amount of PAO in the polar phase relative to the 3 g of PAO in experiments that used equal weights of the PAO and polar solvent. [d]Analyses of the PAO leaching where the PAO leaching is less than 0.03% have to be considered as estimates because of the difficulties in integrating the small PAO signal. [e]Estimates of leaching for this sample of PAO used PAO that was purified by extraction with MeCN for 3 d in a liquid/liquid extraction apparatus. Reprinted with permission from (*52*).

Table 3 shows the mass of PAOs that leached into the various polar solvents as well as the percent leaching of the PAOs in each polar phase. These analyses correspond to the presence of 50-200 ppm of PAO_{687} in any of these solvents. This value would decrease if the PAO were used as a cosolvent. We speculate that the percent leaching of

PAO in these experiments would also be further decreased by the addition of some water or salt to the polar phase. In any case, only a small amount of PAO leached regardless of which polar solvent was used, showing that PAOs as alternative solvents do not significantly contaminate a polar phase in a thermomorphic or biphasic solvent mixture.

As discussed above, prior studies with PE oligomers and with liquid polyolefin cosolvents suggested oligomeric cosolvents could have an additional feature not seen with heptane alone. Specifically, the several cases where our group used PE oligomers as cosolvents as well as the previous experiments detailed studying the leaching behavior of an azo dye and ruthenium bypyridine complex when oligomeric cosolvent was added suggested that oligomers added as cosolvents could reduce hydrocarbon polymer-bound catalyst leaching into a polar phase.[48,50]

To find a suitable dye to study the anti-leaching behavior of oligomeric cosolvents, we next examined the leaching of azo dyes **23**, **24**, **25**, **26**, and **27** shown in Scheme 25 into the polar phase of thermomorphic systems composed of heptane and either methanol, 90% aqueous ethanol, or DMF. These dyes were synthesized using a known procedure also detailed in Scheme 25.[64] In this procedure, 2,6-dimethyl-4-polyisobutylaniline was first prepared by the reaction of alkene-terminated PIB_{1000} with aluminum chloride and 2,6-dimethylaniline in an electrophilic aromatic substitution. After this aniline-terminated PIB was obtained, it was then converted to a diazonium salt by reaction with isoamyl nitrite and boron trifluoride diethyl etherate. The diazonium salt was then further converted to the azo dyes **23-27** by reaction with base and a coupling molecule, for example 2-naphthol.



Scheme 25. Synthesis of PIB-supported azo dyes **23-27** by diazotization and azo coupling reactions.

The dyes **23-27** showed a wide range of leaching behavior (cf. Table 4). The PIB-supported phenol azo dye **23** showed the highest leaching into the polar phase in all of the thermomorphic systems tested, while the PIB-supported resorcinol azo dye **25** showed the lowest leaching. The PIB-supported phloroglucinol dye **26** surprisingly showed higher levels of leaching than the resorcinol dye **25**, suggesting that the number of PIB supports attached is not the only contributor to a reduction in leaching. Both PIB-supported naphthol dye **24** and coumarin dye **27** showed intermediate levels of leaching. Because

the synthesis and purification of the naphthol azo dye **24** was simpler, **24** was chosen as a PIB-bound dye for the following anti-leaching studies with oligomer cosolvents.

Table 4. Leaching of PIB_{1000}-bound azo dyes **23**-**27** into the polar phase of a polar solvent/heptane thermomorphic solvent system.[a]

PIB-supported Azo Dye	Absorbance in 90% Ethanol	Absorbance in Methanol	Absorbance in DMF
23[b]	5.75	9.36	14.1
24	1.00	2.76	3.31
25	0.11	0.25	0.46
26	0.77	0.29	1.03
27	1.29	3.13	3.48

[a]A weight of each dye was added so that the initial concentration in the heptane phase (3 g) was 0.0036 M. 3 g of the polar solvent was also added. Heating to 90 °C produced a thermomorphic solution, which was then cooled down and centrifuged to separate the two phases before the polar phase was analyzed by UV-Visible spectroscopy. [b]The absorbance of the phenol azo dye **23** in any of the three polar solvents was high enough that it required dilution in order to be measured. It was diluted by either a factor of 5 or 10, then multiplied by the dilution factor to give an estimated absorbance.

To carry out these quantitative studies of dye leaching, we first determined the extinction coefficient of 1-(2,4,6-trimethylphenylazo)-2-naphthol, a low molecular weight analogue of **24**, in methanol, 90% aqueous ethanol, DMF, and MeCN so that we could calculate leaching percentages of the dye into the polar phase. Using the extinction coefficients listed in Table 5, we calculated 4.7% leaching of **24** into DMF, 4.1% leaching of **24** into methanol, and 1.3% leaching of **24** into 90% aqueous ethanol. We also calculated 0.9% leaching of **24** into the MeCN phase of a heptane/MeCN biphasic system. While the experiment with MeCN as the polar phase never involved formation of a

homogeneous solution, the 0.9% leaching observed was the limiting value for leaching of **24** after stirring a biphasic mixture of **24**, heptane, and MeCN for 24 h at ambient temperature.

Table 5. Extinction coefficients of 1-(2,4,6-trimethylphenylazo)-2-naphthol in various polar solvents.

Solvent	Extinction Coefficient (M^{-1} cm^{-1})
DMF	19253
Methanol	18417
90% Aqueous Ethanol	20515
MeCN	12617
Heptane[a]	14428

[a]This value is for the PIB-supported naphthol azo dye **24**.

These experiments suggested that the use of **24** with a heptane/methanol thermomorphic mixture would be the most useful system to probe the "anti-leaching" effects of hydrocarbon oligomers, since the dye **24** showed an intermediate amount of leaching into methanol in comparison to the leaching shown when DMF, aqueous ethanol, or MeCN was used in combination with heptane. As shown in Table 6, PIB or PIB-functionalized additives measurably decrease leaching of dye **24** in a thermomorphic system when 20 mg of dye and 1 g of oligomer cosolvent are added to 6 g of a 1/1 (w/w) heptane/methanol thermomorphic system. The identity of the terminal functionality on the PIB has a very small effect on the anti-leaching property of these cosolvents. Similar studies using 2/1/3 (w/w/w) heptane/PAO/methanol systems show that the PAOs are similar to PIB or PIB derivatives as anti-leaching agents.

Table 6. Leaching of polymer-supported azo dye **24** into the methanol phase of a methanol/heptane/polymer cosolvent thermomorphic system.[a]

Entry	Oligomer Cosolvent	Percent Leaching[b]
1	None (heptane only)	4.1
2	PIB-(alkene terminated)	2.3
3	PIB-(CH_2Br terminated)	2.5
4	PIB-(2,6-dimethylaniline terminated)	2.5
5	PIB-(CH_2OH terminated)	2.7
6	PIB-(cresol terminated)	2.8
7	PP	2.3[c]
8	PAO_{687}	1.9[d]
9	PAO_{1758}	2.6[d]
10	PAO_{2505}	3.2[d]

[a]20 mg of **24** and 1 g of the polymer cosolvent were added to 3 g of heptane and 3 g of methanol. Absorbance measurements were taken after thermomorphic heating at 85 °C followed by cooling to room temperature and allowing the samples to sit overnight to separate cleanly. All PIB functionalized materials were prepared from PIB alkene of molecular weight 1000 Da. [b]The percent leaching was calculated by using the known concentration of the dye in heptane and the extinction coefficient of a low molecular weight analogue of the naphthol dye in methanol and has an estimated error of ±0.2%. [c]A similar experiment used 1 g of PP, 2 g of heptane, and 3 g of methanol with a PIB_{2300}-bound naphthol azo dye and had 0.5% dye leaching (0.25 absorbance). [d]This experiment used 20 mg of dye, 1 g of the PAO, 2 g of heptane, and 3 g of methanol. Absorbance measurements of the methanol phase were taken after the mixture was heated at 100 °C to form a single phase and then cooled to room temperature to reform a biphasic mixture. The methanol phase was isolated at that point, centrifuged to remove any physical PAO contaminant, and analyzed. Reprinted with permission from (*52*).

We next set out to more systematically analyze the anti-leaching effectiveness of PAOs as solvents or cosolvents with heptane. Methanol was again chosen as the polar solvent, and the PIB-bound azo dye **24** was used to monitor the leaching in different systems. Similar to the previous experiment, 20 mg of the azo dye **24** were added to the nonpolar phase which had varying amounts of heptane and PAO (3 g total). Next, 3 g of methanol were added and the system was heated to 100 °C to form a monophasic solution as shown in Figure 9. Cooling reformed a biphasic mixture where the dye was visually in

the PAO phase. After separation of the phases, the methanol absorbance was analyzed by UV-Visible spectroscopy to determine the amount of leaching of the azo dye.

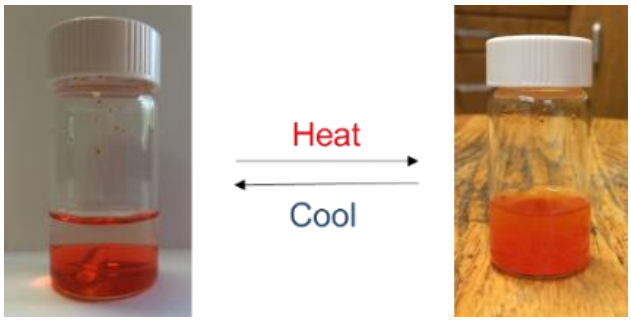


Figure 9. Thermomorphic mixing of PAO_{687} and methanol at 100 ^{o}C. Reprinted with permission from (*52*).

By varying the amount of the PAO with heptane that made up the nonpolar phase, the viability of the PAO as an anti-leaching agent was analyzed. The results of the experiments presented in Table 7 show that as the amount of PAO cosolvent increased in the nonpolar phase, the leaching of the polymer-supported dye **24** into methanol decreased regardless of which molecular weight of oligomer cosolvent was used. PAO_{687} was able to reduce leaching of the dye most significantly as shown in Figure 10. When PAOs were used as replacement solvents for heptane the leaching was reduced even more substantially. Again, PAO_{687} was shown to be the oligomer solvent with the greatest anti-leaching ability.

Table 7. Leaching of the PIB-bound azo dye **24** into the methanol phase of a heptane/PAO/methanol thermomorphic solvent mixture.[a]

PAO	Heptane/PAO Ratio (g/g)	% Leaching of **24** into Methanol[b]
None	3.0/0	4.1
PAO_{2505}	2.0/1.0	3.2
PAO_{2505}	1.5/1.5	2.5
PAO_{2505}	1.0/2.0	2.0
PAO_{2505}	0.5/2.5	1.5
PAO_{2505}	0/3.0	1.1
PAO_{1758}	2.0/1.0	2.6
PAO_{1758}	1.5/1.5	1.7
PAO_{1758}	1.0/2.0	1.5
PAO_{1758}	0.5/2.5	1.1
PAO_{1758}	0/3.0	0.9
PAO_{687}	2.0/1.0	1.9
PAO_{687}	1.5/1.5	1.4
PAO_{687}	1.0/2.0	1.0
PAO_{687}	0.5/2.5	0.8
PAO_{687}	0/3.0	0.6

[a]The dye **24** (20 mg) was added to a heptane/PAO or a PAO only phase (3 g total) followed by the addition of methanol (3 g). This biphasic mixture was then heated to 100 °C. During this heating process, the biphasic mixture became one phase. After stirring for several minutes, the thermomorphic mixture was cooled to room temperature. Centrifugation was used to cleanly separate the phases. The methanol phase was then analyzed by UV−Visible spectroscopy. [b]The leaching value reported is the average of three measurements and was calculated based on the original concentration of the dye in heptane using an extinction coefficient for a low molecular weight analogue of the naphthol dye in methanol. This value has an estimated error of ±0.2%. Reprinted with permission from (*52*).

While the focus of my studies was the synthesis of anti-leaching probes and the study of their behavior in a variety of solvent systems such as PAO/heptane mixtures, our work also included comparisons of reaction rates in heptane and in a PAO to ensure that PAOs behave similarly to heptane as reaction media. This is important because heptane is most commonly used by our group as the nonpolar thermomorphic solvent in catalysis and catalyst recycling. To address this issue, Mr. Thomas Malinski, a coworker, carried

out studies of azo dye isomerization using a PIB-supported ester of *p*-methyl red **28** that had been previously used as an additive in surface modification of polyethylene and as a probe of thermomorphic separations with PIB and polar solvents.[78,79] These studies of the thermal isomerization of **28** in heptane and in PAO_{687} (cf. Scheme 26) showed that the rate of the isomerization remained constant whether heptane or PAO_{687} was used as the solvent. This is illustrated in Figure 11. The isomerization rate in heptane is 2.2×10^{-4} s^{-1} while the rate in PAO_{687} is 2.3×10^{-4} s^{-1}.

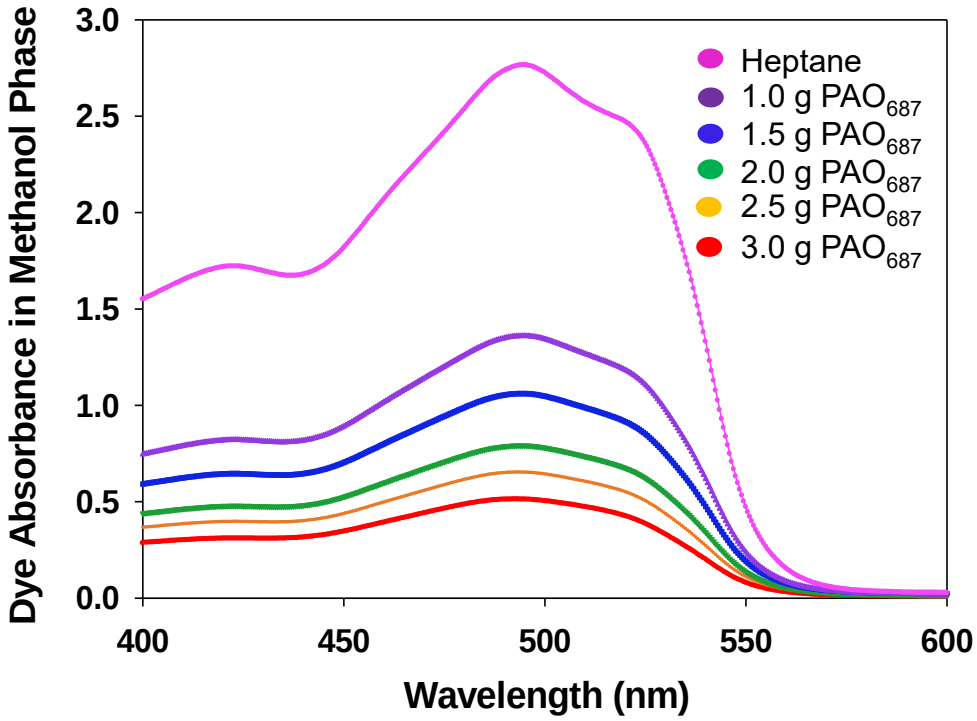
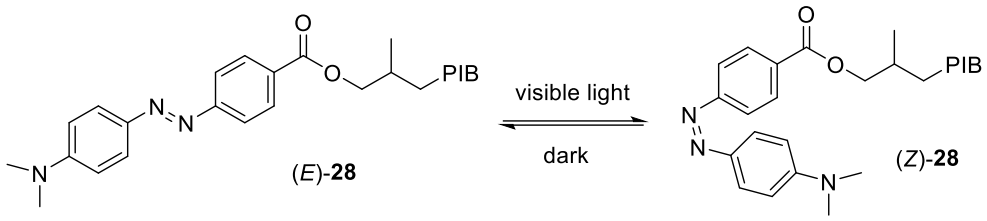


Figure 10. Leaching of PIB-supported naphthol azo dye **24** from 3 g of a heptane/PAO_{687} mixture into methanol (3 g) using a heptane/PAO_{687}/methanol thermomorphic system. Reprinted with permission from (*52*).



Scheme 26. Isomerization of the PIB-supported azo dye **28.**

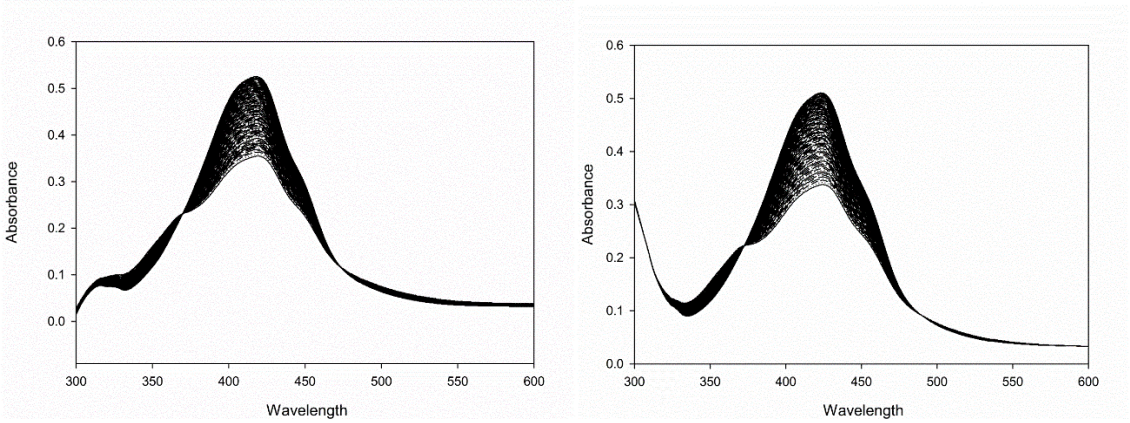


Figure 11. Thermal isomerization of **28** in heptane (left) and in PAO_{687} (right). Reprinted with permission from (*52*).

To further probe the possible difference in reaction rates in heptane and in PAO, Mr. Malinski also examined acid-promoted dye isomerizations in which selected acids were added to study the rate of acid-promoted isomerization of azo dye **28** in both heptane and in PAO_{687}. Regardless of whether the carboxylic acid used was octanoic acid, lauric acid, or a PIB-supported carboxylic acid, the rate of isomerization of **28** increased with acid concentration. The acid-promoted dye isomerization data and the thermal isomerization data showed that these simple reactions in PAO_{687} and in heptane occurred

at similar rates, and that PAOs can serve as a suitable solvent replacement for conventional volatile hydrocarbons.

Finally, we examined recycling of these PAO solvents. These recycling experiments included five cycles for each PAO. Following the protocols used before, we used 20 mg of the dye **24**, 3 g of methanol as the polar solvent, and 3 g of the PAO as the nonpolar solvent. After thermomorphic heating, the solutions were cooled to ambient temperature and UV-Visible spectroscopy was used to analyze the concentration of **24** in the methanol phase of the biphasic mixture. In the second and subsequent cycles, the original methanol phase was removed and 3 g of fresh methanol were added to the PAO phase containing the polymer-supported dye to begin the next cycle. The process was repeated until five cycles were complete. The results presented in Figure 12 show that all of the PAOs can be reused.

Dye leaching slightly decreased during these five cycles. We believe this behavior is similar to leaching behavior seen with catalysts where the first few cycles have more leaching. We believe this occurs because the PIB-bound species has some dispersity where the lower molecular weight fraction has a small but measurably greater leaching rate. No measurable volume decrease of the PAO phase was seen through these five cycles, a result that is consistent with the trace leaching of PAOs into the polar phase. In similar experiments with heptane, the heptane volume would decrease significantly through this same number of cycles unless heptane-saturated methanol was used as the polar phase. Purification of PAO_{1758} and PAO_{2505} by extraction with MeCN for 3 d in a liquid/liquid extraction apparatus had little effect in these experiments. The changes in dye leaching

using purified or "as received" PAO_{1758} and PAO_{2505} were either very small or were within experimental error (Figure 12).

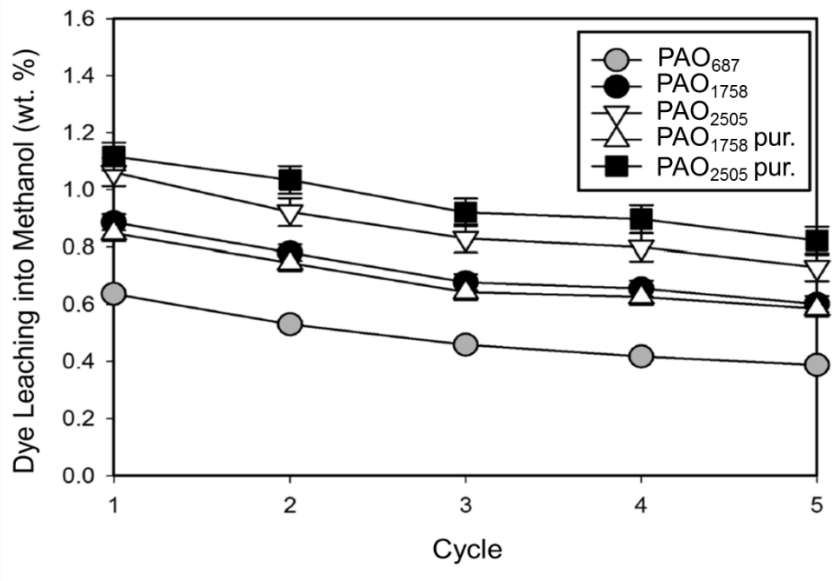


Figure 12. Recycling of PAO solvents in a PAO/methanol thermomorphic solvent system with the azo dye **24**. Reprinted with permission from (*52*).

Conclusions

In summary, the work presented in this chapter shows that hydrocarbon oligomers can be used as alternatives for heptane in thermomorphic solvent systems. Initial studies with a PIB-supported Rh(II) catalyst suggested that these oligomers could be used as cosolvents to help prevent undesired side reactions. Tests with an azo dye and a ruthenium bypyridine complex also suggested that the addition of oligomeric cosolvents such as PIB or PP could reduce leaching of a nonpolar phase selective polymer-supported catalyst into the polar "product" phase of a thermomorphic system. Detailed studies of one class of

oligomeric hydrocarbon solvents, PAOs, show that PAO solvents behave like heptane in terms of their solubility in other solvents and in terms of what they do or do not dissolve. These studies also show that PAOs do not significantly leach into polar phases. In addition, when used with nonpolar phase selective polymer-bound dyes, PAOs act as anti-leaching agents reducing the amount of the polymer-bound dye that leaches into a polar phase. These recyclable oligomeric hydrocarbon solvents were also compared to heptane in studies of azo dye isomerization. The results showed that thermal isomerization or carboxylic acid-promoted isomerization of an azo dye occurs at the same rate in heptane and in a PAO. These results indicate that PAOs and other polyolefin oligomers can be a more sustainable solvent choice in comparison with heptane and that they can serve even better than heptane for separation of soluble polymer-bound catalysts from products in liquid/liquid catalytic recycling systems.

CHAPTER III

SYNTHESIS OF PEG-SUPPORTED AZO AND FLUORESCENT DYES AND STUDIES OF THEIR PHASE SELECTIVITY IN THERMOMORPHIC SOLVENT SYSTEMS

Introduction

Using azo and fluorescent dyes to determine the phase selective solubility of a polymer-supported catalyst in one phase of a thermomorphic or latent biphasic system[80] has been a strategy well-utilized by our group. In thermomorphic and latent biphasic catalytic systems, a monophasic solution is used to carry out the catalytic reaction. By either cooling or perturbation with a third solvent after the conclusion of the reaction, two phases are formed. If the catalyst and the product have high and opposite phase selective solubility, the catalyst can be isolated in one phase and the product in another. If a dye is added onto a polymer support containing a catalyst, the leaching of the catalyst into the less selective phase can be visibly seen (in the case of azo dyes) and the percent leaching can be determined using UV-Visible or fluorescence spectroscopy. For instance, our group has used dye functionalities to analyze the phase selective solubility of the PNIPAM-supported DMAP catalyst **29**,[81] the poly(4-*tert*-butylstyrene)-supported triphenylphosphine catalyst **30**,[82] and the poly(4-dodecylstyrene)-supported DMAP catalyst **31**[83] in these systems (cf. Figure 13).

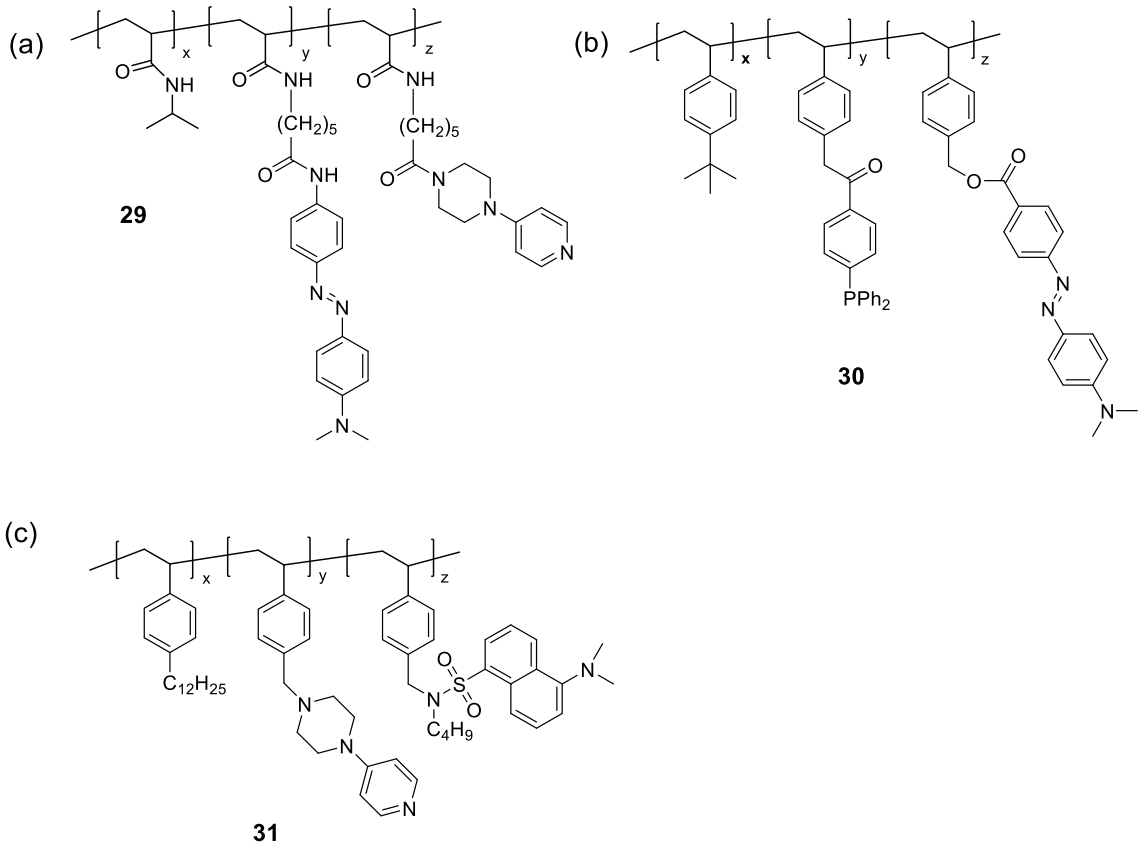


Figure 13. Dye-labeled polymer-supported catalysts including (a) PNIPAM-supported DMAP catalyst **29** used in acylation reactions, (b) poly(4-*tert*-butylstyrene)-supported triphenylphosphine catalyst **30** used in Michael addition reactions, and (c) poly(4-dodecylstyrene)-supported catalyst **31** used in acylation reactions.

If attaching a dye onto the same polymer support as the catalyst cannot be accomplished because the polymer support has only one functionalizable terminus as is the case when using polyisobutylene as a catalyst support, a "catalyst surrogate" can be used to estimate the phase selective solubility of catalysts modified with the same polymer support in a thermomorphic system. The previous chapter describes such a study where a PIB-supported naphthol azo dye was used to predict the leaching of PIB-supported catalysts in thermomorphic systems and how this leaching was minimized by the addition

of PAO polymer cosolvents. Our group also previously reported an example of an azo dye surrogate **32** that determined how phase selective solubility differed when using varying poly(*N*-alkylacrylamide)s as supports (cf. Figure 14).[84]

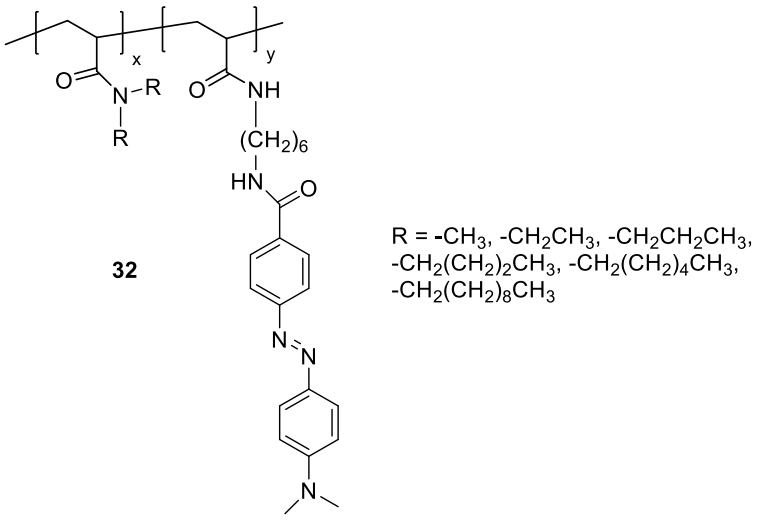


Figure 14. Azo dye **32** used to study the differing phase selective solubility of poly(*N*-dialkylacrylamide) polymer supports in various thermomorphic systems.

This chapter will discuss the synthesis and use of methoxy-terminated PEG (MPEG)-supported azo and fluorescent dyes as surrogates for MPEG-supported catalysts. While a dihydroxy-terminated PEG could in principle be modified to be heterotelechelic, MPEG, like PIB, cannot be easily functionalized by both a dye and a catalyst because it has a methoxy group at one terminus. PEG and its derivatives like MPEG are commonly utilized polymer supports for catalysts and reagents.[9] While the alkyl repeating units of PIB make PIB-bound catalysts phase selectively soluble in nonpolar solvents, the ethylene oxy groups of PEG and MPEG render catalysts soluble in solvents such as ethyl acetate,

THF, DMF, water, acetone, and dichloromethane and insoluble in solvents such as heptane, diethyl ether, and cold isopropanol. This phase selective solubility of PEG-supported catalysts makes them well-suited for thermomorphic systems comprised of a nonpolar solvent like heptane and a more polar solvent such as aqueous ethanol or DMF if products are able to be isolated in a nonpolar phase. Indeed, our group has used thermomorphic systems to recycle PEG-supported catalysts where the products are selectively soluble in a nonpolar phase such as heptane.[13] Such separations are an alternative greener separation process than precipitation, the typical method used to recover and potentially recycle a PEG-supported catalyst. The precipitation method requires the use of large quantities of solvent to precipitate the polymer product, which generates substantial solvent waste compared to the gravity-based separation used with thermomorphic systems (cf. Figure 15).

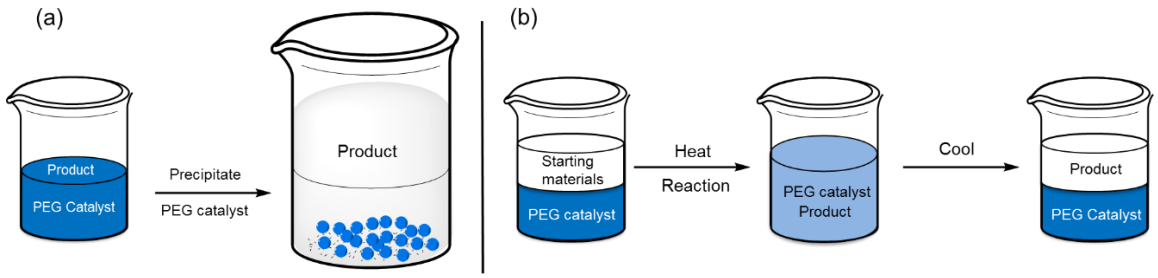
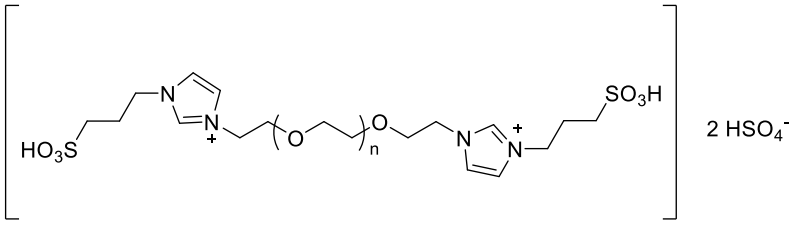


Figure 15. Recycling systems for PEG-supported catalysts including (a) precipitation in a solvent such as diethyl ether followed by filtration or (b) a thermomorphic system involving a gravity-based separation after the catalytic reaction.

Because previous work in our group as well as previous work discussed in this dissertation involves the addition of polymer cosolvents to reduce leaching of polymer-

supported catalysts into the non-selective phase of a recyclable system,[48] we were also interested in studying the effect of added PEG on thermomorphic systems using PEG-supported dyes as catalyst surrogates. PEG is perhaps the most commonly utilized polymer solvent, and has been used as a medium for catalytic reactions including Sonogashira[85] and Suzuki-Miyaura[86] coupling, enantioselective reductions with a ruthenium-incorporated BINAP catalyst,[47] and C-S coupling of thiols.[46] Additionally, in 2009 Luo reported the use of a thermomorphic recycling system of PEG-supported ionic liquid **33** and toluene.[87] In this system, three-component condensation reactions of aromatic aldehydes, activated methylene compounds, and 5,5-dimethyl-1,3-cyclohexanedione could be carried out as shown in Scheme 27. The resulting benzopyrans were obtained in >82% yield after 1.5 h and in the reaction of 4-nitrobenzaldehyde, malononitrile, and 5,5-dimethyl-1,3-cyclohexanedione, the PEG-supported ionic liquid **33** could be used for 10 cycles without an obvious loss of activity and <10% weight loss of **33**. This result and the use of PEG as a common polymer reaction medium suggested to us that PEG could also act as an anti-leaching cosolvent in our studies.



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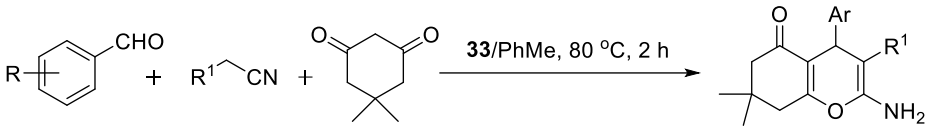
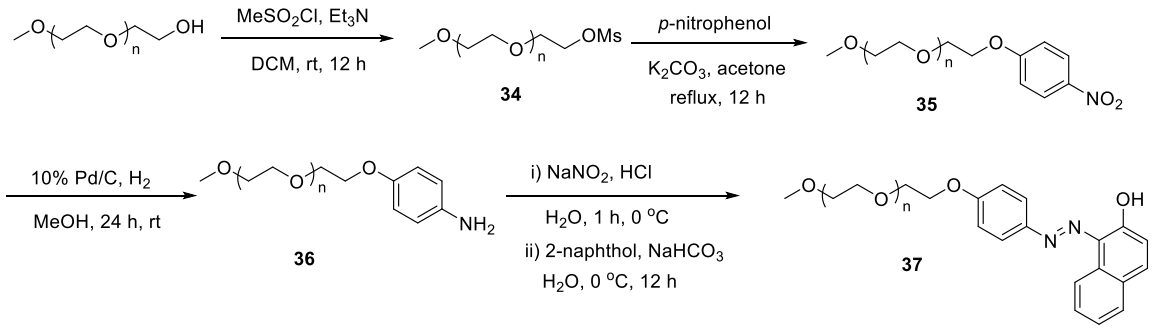


Scheme 27. Three-component condensation reactions using a PEG-supported ionic liquid/toluene thermomorphic solvent system.

Results and Discussion

To begin this work, we first synthesized the PEG-supported naphthol azo dye **37** by modification of literature procedures, as depicted in Scheme 28.[88,89] The PEG_{2000} monomethyl ether starting material was first converted to the mesylate-terminated PEG monomethyl ether **34** using methanesulfonyl chloride and triethylamine. The resulting oligomer **34** was next allowed to react with *p*-nitrophenol and potassium carbonate to give the 4-nitrophenyl-terminated PEG monomethyl ether **35**. Reduction of **35** with Pd/C and hydrogen gave the 4-aminophenyl-terminated PEG monomethyl ether **36**. Finally, **36** was converted to the PEG-supported azo dye **37** by diazotization with sodium nitrite and hydrochloric acid followed by an azo coupling reaction with 2-naphthol and sodium bicarbonate. The PEG-supported azo dye **37** was obtained as a powdery red solid which was purified by recrystallization in isopropanol. We next attempted to analyze the phase selectivity of the PEG_{2000}-supported naphthol dye in thermomorphic mixtures of heptane

with DMF, 90% aqueous ethanol, or methanol. As shown in Figure 16, no visual leaching of the dye into the heptane phase was observed when using any of the three polar solvents with heptane. Leaching was also undetectable when using UV-Visible spectroscopy to analyze the heptane phase.



Scheme 28. Synthesis of PEG-supported naphthol azo dye **37**.

Because no leaching was observed when using PEG_{2000} as a polymer support, we next attempted to synthesize the PEG_{750}-supported azo dye. However, the synthesis of the 4-nitrophenyl-terminated PEG_{750} monomethyl ether was much more challenging because of the inability to use precipitation or recrystallization, common purification methods for the synthesis of PEG-supported materials. However, a control experiment with $MPEG_{750}$ and *p*-nitrophenol showed that stirring with barium hydroxide was able to remove the nitrophenol as a barium salt, while the MPEG remained soluble in DCM. This procedure worked to remove phenol and *p*-methylphenol from $MPEG_{750}$ as well. We believe this technique can later be applied to purification of the 4-nitrophenyl-terminated PEG monomethyl ether and the PEG-supported naphthol dye by removal of the low molecular

weight compounds as barium salts. This technique could allow for the preparation of an azo dye catalyst surrogate with a lower molecular weight PEG support.

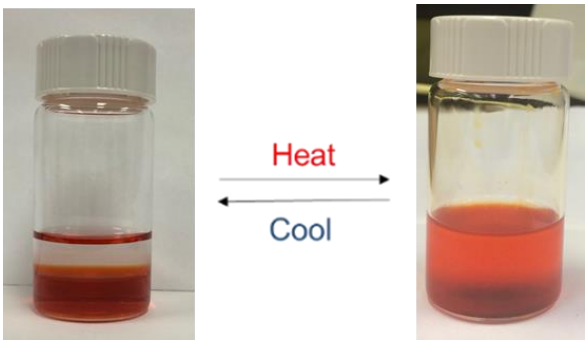
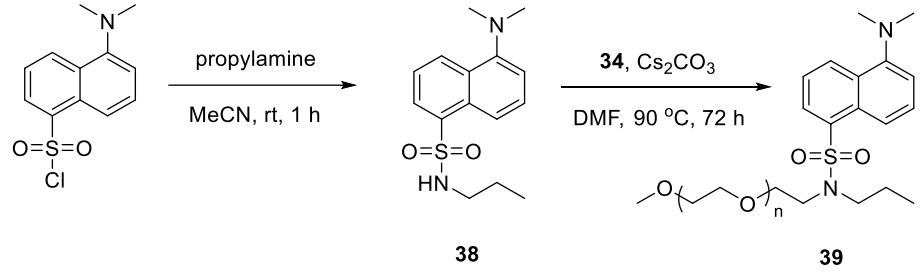


Figure 16. Thermomorphic mixing of heptane and DMF at 90 ºC with PEG-supported azo dye **37**.

Because of the high phase selective solubility of **37** in polar solvents and an inability to detect any leaching of the azo dye into the heptane phase of a thermomorphic system, we also prepared the dansyl-terminated PEG monomethyl ether fluorophore **39** as a more sensitive probe which could be used as a catalyst surrogate. This fluorophore-labeled PEG derivative was easily prepared in two steps as shown in Scheme 29. To prepare **39**, dansyl chloride was first allowed to react with propylamine using a known procedure to give the dansyl derivative **38**.[90] Mesylate-terminated PEG_{2000} monomethyl ether **34**, prepared using the same method previously described, was then converted to the dansyl-terminated PEG monomethyl ether dye **39** by reaction with **38** and cesium carbonate.[91] The fluorophore **39** was purified by precipitation in diethyl ether or recrystallization in isopropanol and was then analyzed by fluorescence spectroscopy. Table 8 shows the emission λ_{max} of **39** in solvents commonly used in thermomorphic

systems. The λ_{max} of **39** in polar solvents such as DMF, methanol, and 90% aqueous ethanol did not vary much, only ranging from 520-524 nm. However, a significant hypsochromic shift was observed when heptane was used as the solvent, giving a λ_{max} of 492 nm. This hypsochromic shift was even more significant for the low molecular weight dansyl dye **38**, with the λ_{max} changing from 507 nm in DMF to 448 nm in heptane.



Scheme 29. Synthesis of PEG-supported fluorophore **39**.

Table 8. Emission λ_{max} of the PEG_{2000}-supported dansyl dye **39** in various solvents.[a]

Fluorophore	Concentration (M)	Solvent	λ_{max} (nm)
39	3.6×10^{-6}	Methanol	524
39	3.6×10^{-6}	90% Aq. Ethanol	520
39	6.3×10^{-6}	DMF	521
39	--[b]	Heptane	492
38	9.6×10^{-7}	DMF	507
38	9.6×10^{-7}	Heptane	448

[a]All of the samples were measured using an excitation wavelength of 357 nm. [b]This value for the λ_{max} of the PEG_{2000}-supported dansyl dye in heptane was taken from the leaching of **39** into heptane from DMF after thermomorphic mixing at 90 °C.

After the PEG_{2000}-supported dansyl dye **39** was synthesized, we attempted the synthesis of PEG-supported dansyl dyes with lower molecular weight PEG supports. This work was carried out with Mr. Jonas Bianga, a visiting scholar from the Technical University of Dortmund in Germany. Mr. Bianga successfully developed a chromatographic purification method for the synthesis of PEG-supported dansyl dyes with PEG supports of M_n 750 and 1000 Da. PEG-supported dansyl dyes with supports of M_n 2000 and 5000 Da were also synthesized and then purified by precipitation in diethyl ether. He and I then conducted studies in collaboration of these PEG-supported dansyl dyes' leaching into the heptane phase of thermomorphic systems comprised of heptane and DMF. After thermomorphic mixing at high temperature, the phases were cooled and separated and the DMF layer was diluted by a factor of 1000. The heptane and DMF layers were then analyzed by fluorescence spectroscopy using an excitation wavelength of 357 nm. The ratio of the intensities for the heptane and DMF phases considering the DMF dilution factor was then used to calculate the percent leaching of the dansyl dye **39** into the heptane phase.

Initial results showed that the molecular weight of the polymer support of **39** altered the percent leaching into the heptane phase. While PEG_{5000}- and PEG_{2000}-supported dansyl dyes had similar percent leaching into heptane when using 0.02 mmol of the dye (0.0010% and 0.0012%), the lower molecular weight PEG_{1000}- and PEG_{750}-supported dansyl dyes showed increasingly greater leaching into the heptane phase (0.006% and 0.024%). This result was expected because increasing the molecular weight of the polymer support usually produces an increase in phase selective solubility and a reduction in

leaching. For instance, PIB-supported azo dye catalyst surrogates were also shown to increase their phase selectivity in heptane upon an increase of the molecular weight of the polymer support.

A temperature of 90 ^{o}C was used for the majority of these studies because heptane and DMF are miscible at that temperature. No substantial change in the leaching into the heptane phase was observed for the PEG_{5000}-, PEG_{2000}-, and PEG_{1000}-supported dansyl dyes when the temperature was raised to 110 ^{o}C. However, for the PEG_{750}-supported dansyl dye, a slight increase in the leaching from 0.024% to 0.040% was noted. The PEG_{750}-supported dansyl dye was also studied to test whether the time of heating had an effect on the percent leaching. However, the leaching into heptane remained constant regardless of the time heating at 90 ^{o}C, as shown in Table 9.

We next investigated the effect of added unfunctionalized MPEG on the leaching of PEG-supported dansyl dyes into the heptane phase of heptane/DMF thermomorphic systems. The results shown in Table 10 indicated that the addition of MPEG does not significantly affect the leaching of PEG_{5000}-, PEG_{2000}-, and PEG_{1000}-supported dansyl dyes into the heptane phase. In contrast, an increase in leaching into the heptane phase was observed for the PEG_{750}-supported dansyl dye when MPEG was added. When a 1:1 ratio of **39** to MPEG was used, the leaching of the dye into heptane increased from 0.024% to 0.035%. This leaching value further increased when using a 1:10 ratio (0.042%) and a 1:25 ratio (0.056%). However, no substantial change in leaching was seen between a 1:25 ratio and a 1:100 ratio, indicating that the leaching value of **39** into heptane stabilizes at a 1:25 ratio of the PEG-supported dansyl dye to added MPEG. There was also no noticeable

change observed in the leaching of PEG_{750}-supported **39** into heptane when $MPEG_{5000}$, a less hygroscopic polymer, was added instead of $MPEG_{750}$. This result suggested that the addition of a minor amount of water does not significantly change the leaching behavior.

These results showed that while MPEG does not act as an "anti-leaching" agent like the PAOs mentioned in the last chapter, it could still serve as a viable and green alternative cosolvent for PEG-supported catalysts with polymer supports of 1000 Da or higher. MPEG is less toxic and less flammable than DMF, which may have long-term effects on liver function and reproduction.[92]

Table 9. Leaching of the PEG_{750}-supported **39** into the heptane phase of a heptane/DMF thermomorphic system.

Time Heating (min)	Leaching into Heptane (%)
2	0.024
5	0.028
15	0.023
60	0.027

[a]The dye **39** (0.02 mmol) was added to 3 g of DMF and 3 g of heptane. This biphasic mixture was then heated to 90 °C to form one phase. After stirring for several minutes, the thermomorphic mixture was cooled to room temperature. Centrifugation was used to cleanly separate the phases. The heptane and diluted DMF phases were then analyzed by fluorescence spectroscopy. [b]The leaching value reported is the average of two measurements and was calculated using the ratio of the intensities in the two phases.

Table 10. Addition of MPEG to PEG-supported dansyl dyes in a heptane/DMF thermomorphic solvent system.[a]

M_n of **39** Support (Da)	Ratio of **39** to Added PEG	Leaching into Heptane (%)
750	No added PEG	0.024
750	1:1	0.035
750	1:10	0.042
750	1:25	0.056
750	1:100	0.057
1000	No added PEG	0.006
1000	1:1	0.006
1000	1:10	0.008
2000	No added PEG	0.001
2000	1:1	0.001
2000	1:10	0.001
5000	No added PEG	0.001
5000	1:1	0.001
5000	1:10	0.001

[a]The dye **39** (0.02 mmol) and unfunctionalized MPEG of the same molecular weight as **39** was added to 3 g of DMF and 3 g of heptane. This biphasic mixture was then heated to 90 °C to form one phase. After stirring for several minutes, the thermomorphic mixture was cooled to room temperature. Centrifugation was used to cleanly separate the phases. The heptane and diluted DMF phases were then analyzed by fluorescence spectroscopy. [b]The leaching value reported is the average of two measurements and was calculated using the ratio of the intensities in the two phases.

We also studied how the addition of unfunctionalized MPEG altered the percent leaching of DMF into the heptane phase. ^{1}H NMR spectroscopic analyses were carried out comparing the ratio of the heptane -CH_3 peak at δ 0.9 to the DMF formamide peak at δ 8.0 when an aliquot of the heptane phase was collected after thermomorphic mixing. These results showed that as the amount of added $MPEG_{750}$ increased from 0.06 to 0.14 to 0.34 mmol, the leaching of DMF into heptane decreased from 2.7% to 2.4% to 2.3%. These values were slightly lower than the initial leaching value obtained without the addition of

MPEG (3.6%), which indicates that PEG can slightly prevent the leaching of DMF into the heptane phase. This could be a benefit if a PEG/DMF phase was used in a thermomorphic system because it would allow for slightly greater recyclability of the DMF solvent over multiple cycles.

Conclusions

This chapter reported the synthesis of PEG-supported fluorescent and azo dyes for use as catalyst surrogates. A new procedure was developed for the synthesis of a PEG-supported naphthol azo dye but unfortunately the PEG_{2000}-supported dye did not have detectable leaching into the nonpolar phase of thermomorphic systems so it was not used as a catalyst surrogate. PEG-supported dansyl dyes with M_n of 750, 1000, 2000, and 5000 Da were then synthesized and all four molecular weights of the dye were detectable by fluorescence spectroscopy. This dye was thus employed as a catalyst surrogate for the following studies.

Leaching of the PEG-supported dansyl dye was dependent on the molecular weight of the polymer support. The PEG_{750}-supported dansyl dye showed the greatest leaching into the heptane phase while the PEG_{5000}- and PEG_{2000}-supported dansyl dyes showed the least. The leaching of the PEG_{750}-supported dansyl dye into heptane was not altered by the heating and stirring time, although an increase in leaching was observed when the temperature was increased. The addition of unfunctionalized MPEG did not significantly affect the leaching of the PEG_{5000}-, PEG_{2000}-, and PEG_{1000}-supported dansyl dyes into the heptane phase, although an increase in the leaching into heptane was observed for the

PEG_{750}-supported dansyl dye which stabilized at 0.06% after a 25:1 ratio of MPEG to the dansyl dye was used. ^{1}H NMR spectroscopic analyses showed that the leaching of DMF into heptane was slightly decreased by the addition of MPEG, although the leaching of the added MPEG into the heptane phase may be problematic. However, the results showed potential for MPEG to be used as a cosolvent for thermomorphic systems containing catalysts with a PEG support of 1000 Da or higher.

CHAPTER IV

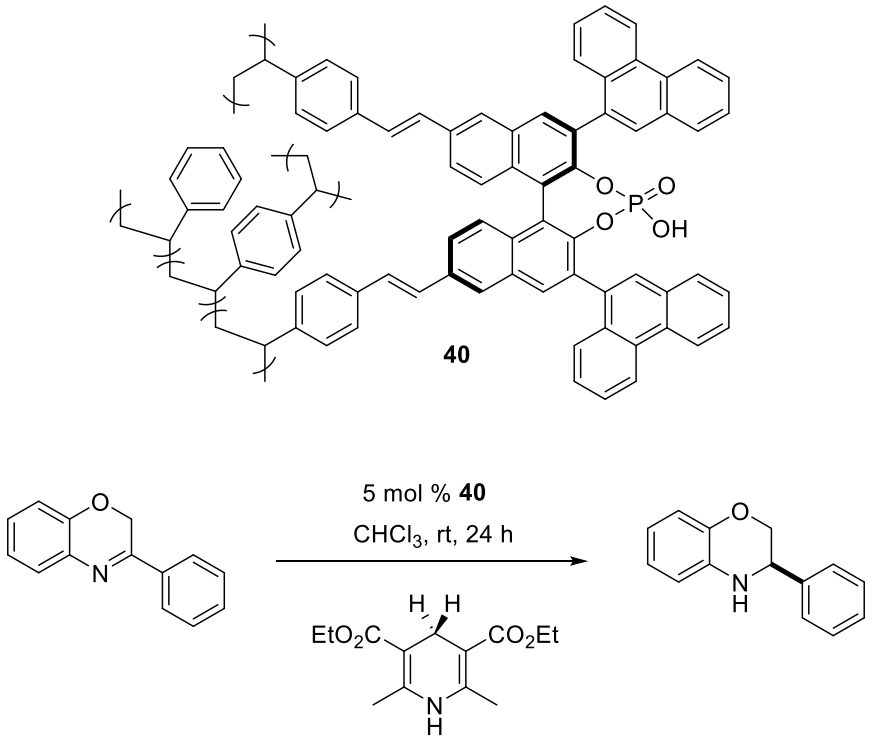
SYNTHESIS OF PIB-SUPPORTED BINOL LIGANDS AND THEIR USE IN CATALYTIC REACTIONS

Introduction

In the last two decades, interest in asymmetric catalysis has greatly increased because of the potential for the asymmetric compounds generated to be used in various applications such as pharmaceuticals, where obtaining a pure enantiomer of a compound is necessary. A variety of chiral ligands have been developed for this purpose, but the enantiomers of 1,1'-bi-2-naphthol (BINOL) and its derivatives have been well-studied because of their versatility.[93] These BINOL ligands have been used in a variety of asymmetric reactions including organozinc addition to aldehydes,[94,95] epoxidation,[96] and the Morita-Baylis-Hillman reaction.[97,98] The phosphoric acid derivative of BINOL has also been well-studied and its use as a catalyst for the Mannich reaction,[99,100] the Nazarov cyclization,[101] the Biginelli reaction,[102] and for hydrogenation[103] has been documented.

The attachment of polymer supports on asymmetric catalysts such as these BINOL ligands has also been investigated.[104] Crosslinked PS[105–108] as well as soluble polymers such as PEG[109] and PNIPAM[110] have been used as supports for BINOL. One example is the PS-supported BINOL phosphoric acid catalyst **40** reported by Sugiono.[108] This catalyst was prepared by the terpolymerization of a (*R*)-BINOL phosphoric acid containing styrene groups with styrene and divinylbenzene. The crosslinked PS-supported catalyst (*R*)-**40** (5 mol %) was then used in asymmetric hydrogenation reactions of a benzoxazine using

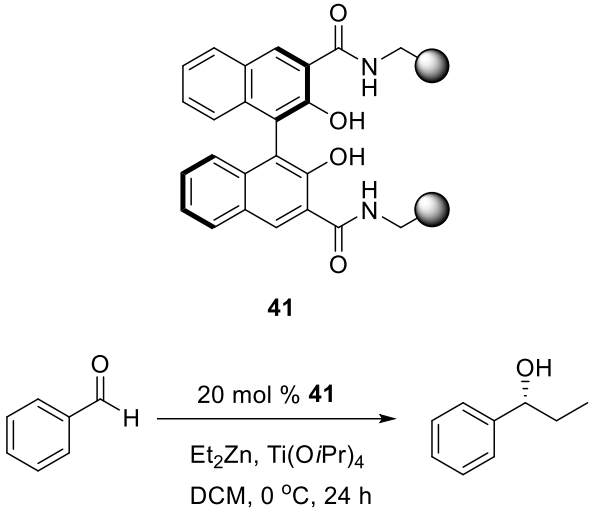
Hantzsch dihydropyridine as a hydride source as shown in Scheme 30. Importantly, this catalyst was recyclable for the hydrogenation, giving >85% yield of the product with a consistent 94% *ee* for 12 cycles. Because of the heterogeneous support, the catalyst was easily recovered and reused after each cycle by filtration and washing with chloroform.



Scheme 30. Hydrogenation reactions of a benzoxazine using the PS-supported (*R*)-BINOL phosphoric acid catalyst **40**.

Wang and Chan also reported the use of a PS-supported BINOL ligand for titanium-catalyzed diethylzinc addition to aldehydes.[106] This ligand **41** was prepared by the coupling reaction of an aminomethylated PS resin with (*R*)-2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid. The (*R*)-BINOL ligand **41** (20 mol %) was then

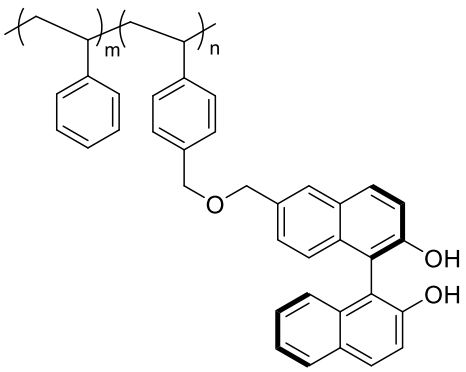
used in the diethylzinc addition reaction of benzaldehyde with titanium isopropoxide to give the alcohol product in 93% isolated yield with 97% *ee* as shown in Scheme 31. They also investigated the use of a homogeneous analogue of **41** with -$CONHCH_2Ph$ groups at the 3,3'-positions of BINOL. In the same reaction, less time was required (12 h instead of 24 h) and the yield was comparable but a lower *ee* (67%) was obtained. However, no recycling of the PS-supported **41** was reported.



Scheme 31. Diethylzinc addition to benzaldehyde using the PS-supported (*R*)-BINOL ligand **41** with titanium isopropoxide.

Yet another example of a PS-supported BINOL ligand was reported by Sasai.[111] This ligand **42** was synthesized by the copolymerization of a styrene-containing (*R*)-BINOL ligand with styrene and was used with triisopropoxyytterbium in the asymmetric epoxidation of enones, as shown in Scheme 32. When 4-phenylbut-3-en-2-one was used as the starting material, the BINOL ligand **42** could be recycled in the epoxidation reaction

after washing with ether and THF giving the product in reduced yield (62% for the second cycle vs. 90% for the first cycle) with a comparable *ee* (89% vs. 88%). A third cycle could also be completed by increasing the reaction time to 36 h and this cycle gave a similar yield of product and comparable *ee* to the second cycle.



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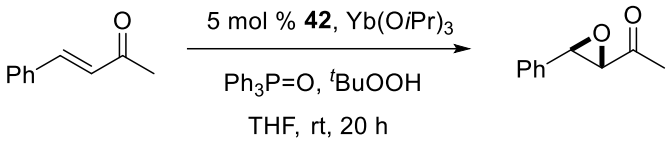
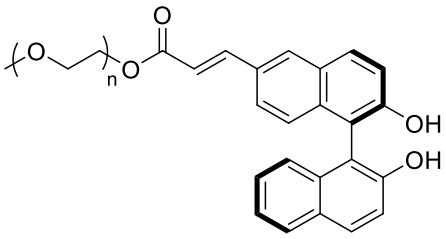


Scheme 32. Epoxidation of enones using the PS-supported (*R*)-BINOL ligand **42** with triisopropoxyytterbium, triphenylphosphine oxide and *tert*-butyl hydroperoxide.

A PEG-supported BINOL ligand was also reported by Zimmer.[109] This ligand **43** was prepared by the Heck reaction of (*R*)-6-bromo-[1,1'-binaphthalene]-2,2'-diol with an acrylate-terminated PEG monomethyl ether using palladium acetate. Ligand **43** (10 mol %) was then successfully used with titanium isopropoxide and an (*S*)-prolinol derivative as an additive in the Mukaiyama aldol reaction of 2-styryl-oxazole-4-carbaldehyde with a

S-ketene silyl acetal to give the corresponding product in 63% yield and 94% *ee*. Without the addition of the prolinol derivative, the product could be obtained in 93% yield with an *ee* of 78% after 24 h. However, when **43** was recovered by precipitation in diethyl ether and reused, the enantioselectivity of the product decreased to 70% *ee* and the yield decreased significantly to 35%.



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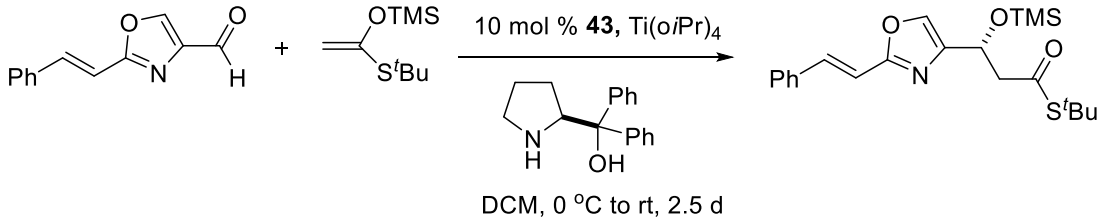


Scheme 33. Mukaiyama aldol reaction of 2-styryl-oxazole-4-carbaldehyde and a S-ketene silyl acetal using MPEG-supported (*R*)-BINOL ligand **43**, titanium isopropoxide, and a (*S*)-prolinol derivative as an additive.

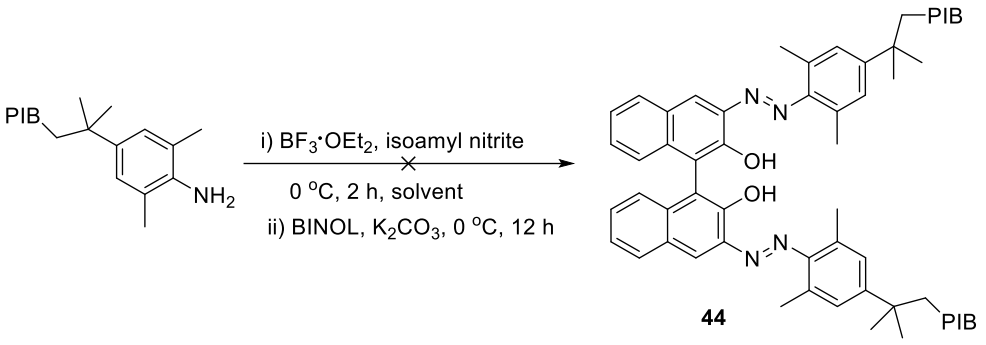
Because our group has designed a variety of polymer-supported catalysts and ligands and because the work described previously had successfully developed new solvents and new phase separation strategies, we were interested in synthesizing an alkane soluble polymer-supported BINOL ligand for use in a homogeneous catalytic system that could be separated and recycled using similar chemistry. We chose to use PIB as a polymer

support to attach to BINOL because of our experience preparing catalysts and dyes with this same support that are nonpolar phase selectively soluble when a biphasic separation with a polar solvent and a nonpolar solvent is used. Since many of the reactions that use BINOL as a catalyst produce polar phase selectively soluble products, we hoped that this sort of phase selective solubility of the PIB support could allow us to recover and reuse a PIB-supported BINOL ligand by a simple extraction. We hoped that this simpler procedure would be better able to preserve the yield and enantioselectivity of the product through multiple cycles in comparison with recycling procedures used with other polymer-supported BINOL ligands.

Results and Discussion

While this work is still incomplete, we studied a number of routes to a potential PIB-supported BINOL ligand using several different synthetic methods. The first method we tried was to attach PIB by the azo coupling of racemic BINOL with a PIB-supported phenyl diazonium salt, a reaction we had previously used (cf. Chapter II) to prepare a PIB-supported naphthol azo dye.[64] Unfortunately, the synthesis of the PIB-supported BINOL azo dye **44** shown in Scheme 34 failed when using DCM and THF as the solvent. Even when ethyl acetate or methanol were used with DCM to try to better solubilize the BINOL (2:1 ratio of either solvent to DCM), the reaction still showed no conversion to the azo dye. This result suggests that the reactivity of BINOL is much lower in azo coupling reactions than other aromatic compounds such as naphthol and phenol in solvents that are suitable for the PIB-supported diazo electrophile.

Alternative procedures have been developed in our group since these initial experiments that make a phenolate anion phase selectively soluble in heptane by the preparation of a salt of tetrabutylammonium phenolate from phenol and tetrabutylammonium hydroxide. A similar approach could make it possible to prepare a BINOL anion that upon formation of the tetrabutylammonium salt would show increased solubility in heptane or other nonpolar solvents and could react with the PIB-supported diazo compound. This strategy would be advantageous because experiments we did showed that BINOL is not soluble in toluene, a similarly nonpolar solvent, at room temperature or at 0 ^{o}C, temperatures required for the azo coupling reaction. If the BINOL anion could be solubilized in heptane or hexanes, the reaction could then be attempted in a suitable solvent for both the PIB-supported diazo compound and BINOL.

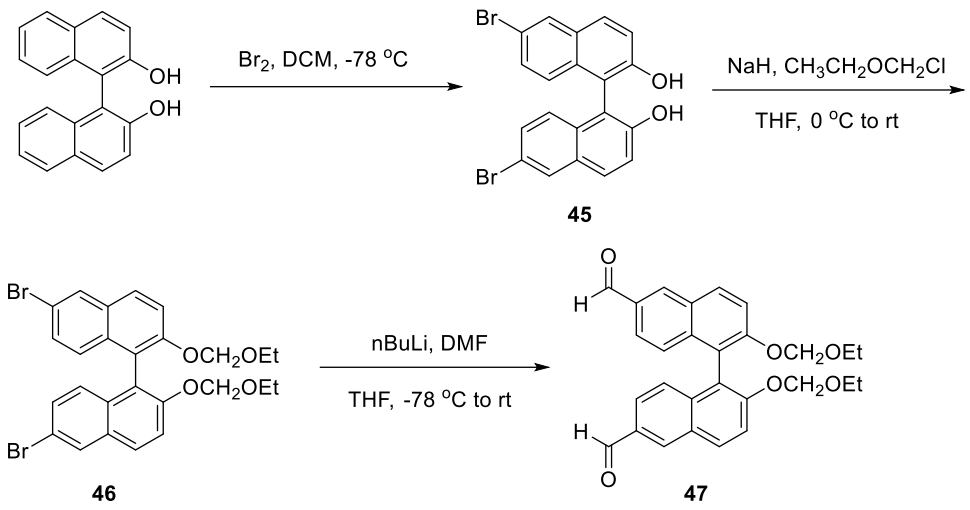


Scheme 34. Synthesis of the PIB-supported BINOL azo dye **44**.

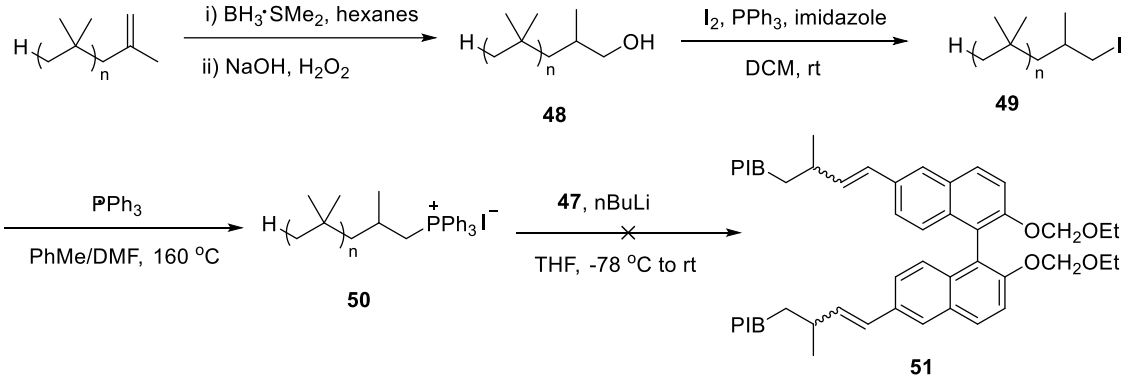
We next attempted to synthesize a PIB-supported BINOL ligand by the Wittig reaction of a BINOL dialdehyde with a phosphonium salt-terminated PIB using literature procedures reported by our group and others.[108,112,113] The BINOL dialdehyde **47** was

prepared in three steps as shown in Scheme 35. First, racemic BINOL was allowed to react with bromine to give the BINOL derivative **45** modified with bromo groups at the 6,6'-positions. Next, the two hydroxyl groups of this dibrominated **45** were protected using chloromethyl ethyl ether to give **46**. The protected dibrominated BINOL **46** was then allowed to react with *n*-butyllithium and DMF to give the modified BINOL **47** containing aldehyde groups at the 6,6'-positions.

The phosphonium salt-terminated PIB **51** was then prepared as shown in Scheme 36.[113] First, alkene-terminated PIB was allowed to react with boron dimethylsulfide, sodium hydroxide, and hydrogen peroxide in a hydroboration/oxidation reaction to give the alcohol-terminated PIB **48**. This alcohol **48** was then converted to the corresponding iodide-terminated PIB **49** using iodine, triphenylphosphine, and imidazole. The iodide-terminated PIB **49** was next converted to the phosphonium-salt terminated PIB **50** by reaction with triphenylphosphine. The triphenylphosphonium iodide salt **50** was then allowed to react with *n*-butyllithium and the BINOL dialdehyde **47** in a Wittig reaction. Unfortunately, attempts to prepare the BINOL ligand **51** with polyisobutyl groups at the 6,6'-positions failed. This suggests that the BINOL dialdehyde **47** is less reactive under these conditions than 4-bromobenzaldehyde, which our group previously used with the same phosphonium salt **50** in a Wittig reaction to prepare the 4-bromophenyl-terminated PIB.[113] The BINOL dialdehyde **47** can be further modified with substituents such as bromo or nitro groups to test whether the presence of an electron-withdrawing substituent can increase the reactivity of the dialdehyde.



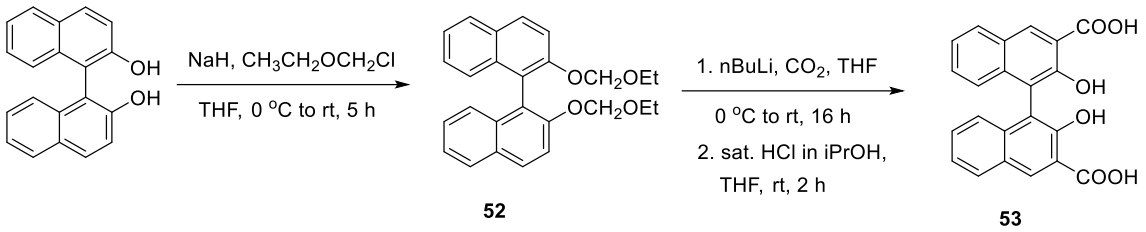
Scheme 35. Synthesis of 2,2'-bis(ethoxymethoxy)-[1,1'-binaphthalene]-6,6'-dicarbaldehyde **47.**



Scheme 36. Synthesis of the PIB-supported BINOL ligand **51.**

Our next attempt to attach PIB supports onto BINOL was modified from the synthesis of the PS-supported BINOL ligand **41**.[106] To begin this synthesis, we first prepared the BINOL derivative **53** modified with carboxylic acid groups at the 3,3'-

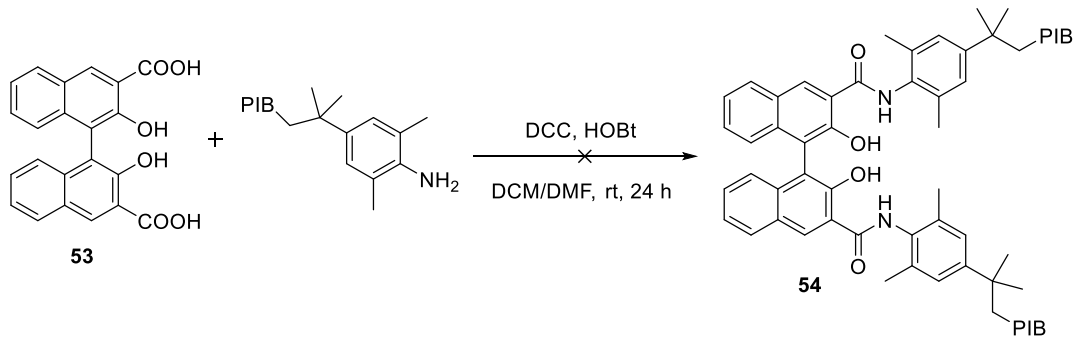
positions as shown in Scheme 37. First, the two hydroxyl groups of racemic BINOL were protected using chloromethyl ethyl ether to give the protected BINOL **52**. This BINOL derivative **52** was then allowed to react with *n*-butyllithium and carbon dioxide followed by deprotection with concentrated HCl to give the BINOL dicarboxylic acid **53**.



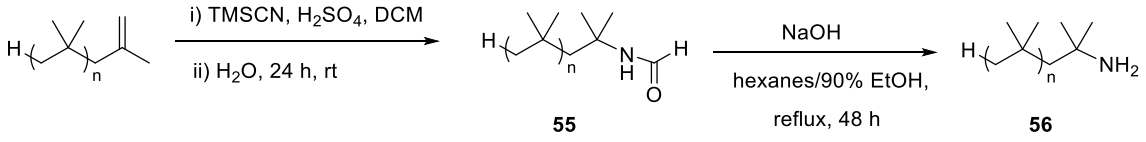
Scheme 37. Synthesis of the 2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid **53.**

This BINOL dicarboxylic acid **53** was then tested in a coupling reaction with a 2,6-dimethylaniline-terminated PIB previously used as a precursor for the synthesis of PIB-supported azo dyes as shown in Scheme 38.[64] Unfortunately, the coupling of the aniline-terminated PIB and the BINOL dicarboxylic acid **53** failed when using DCC and hydroxybenzotriazole (HOBt), the condition reported for the synthesis of the PS-supported BINOL ligand **41**. Allowing **53** to react with oxalyl chloride followed by the addition of triethylamine and the aniline-terminated PIB also failed to give the PIB-supported BINOL ligand **54**. Because we wanted to use an achiral amine like the aniline-terminated PIB to avoid any effect on the enantioselectivity if we later used a modified (*R*)- or (*S*)-BINOL to couple to PIB, we considered modifying the synthesis of an achiral amine earlier reported by our group.[114] However, this synthesis required multiple steps in

addition to the synthesis of the BINOL dicarboxylic acid **53**. For this reason, we instead used a procedure to prepare a formamide-terminated PIB which was developed by Dr. Jakkrit Suriboot, a previous member of our group. In this synthesis, the formamide-terminated **55** was prepared by the reaction of alkene-terminated PIB with trimethylsilyl cyanide, sulfuric acid, and water. The formamide-terminated PIB **55** was then hydrolyzed with sodium hydroxide to give the achiral amine-terminated PIB **56**, as shown in Scheme 39.



Scheme 38. Synthesis of the PIB-supported BINOL ligand **54**.

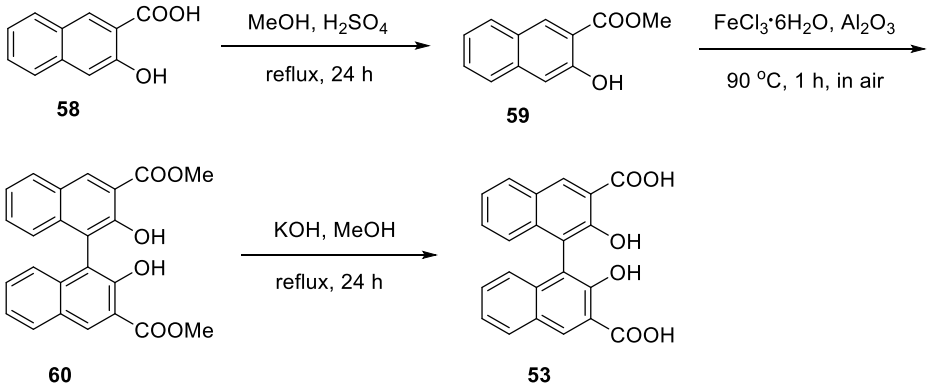


Scheme 39. Synthesis of the amine-terminated PIB **56.**

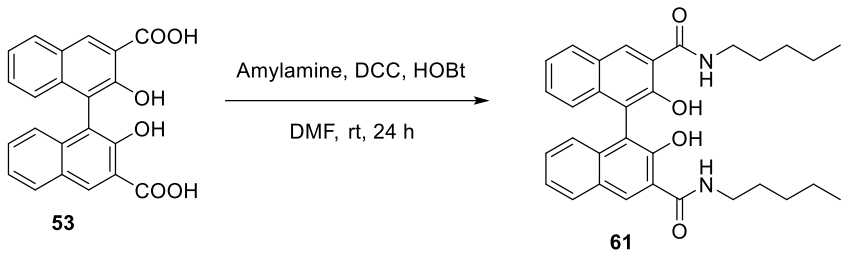
When the amine-terminated PIB **56** was used in a coupling reaction with the BINOL dicarboxylic acid **53**, DCC, and HOBt, the PIB-supported BINOL ligand **57** was successfully obtained as shown in Scheme 40. Since our ultimate goal was to use ligands like **57** as phase separable supports, we initially examined the phase selective solubility of **57**. Gratifyingly, this ligand **57** showed >99% phase selective solubility in either heptane or PAO_{687} versus DMF after heating under thermomorphic conditions followed by cooling and separation of the two phases. This value was calculated by a ^1H NMR experiment with the DMF phase which measured the integration of an $MPEG_{2000}$ internal standard at δ 3.6 relative to the integration of the $-CH_2$ peak of the repeating unit of PIB at δ 1.4. When a Baylis-Hillman catalytic reaction was later conducted and the PIB-supported BINOL ligand **57** and the products were separated using a heptane/MeCN biphasic system, the MeCN phase also showed no peaks attributable to **57**, again indicating the high phase selective solubility of this ligand in heptane versus polar solvents like MeCN.

Scheme 40. Synthesis of the PIB-supported BINOL ligand **57.**

However, while **57** had the desired phase selective solubility, it was difficult to prepare a substantial amount of **57** because of the low yield obtained for the BINOL dicarboxylic acid **53** due to the extensive workup procedure. For this reason, a more facile synthesis of **53** previously reported in the literature was also then investigated, as shown in Scheme 41.[115,116] In this synthesis, 2-hydroxy-3-naphthoic acid was first converted to the corresponding methyl ester by esterification with methanol. The methyl ester **59** was then allowed to react with iron (III) chloride hexahydrate on alumina in an oxidative coupling reaction to give the BINOL derivative **60** with methyl ester groups at the 3,3'-positions. Finally, hydrolysis of **60** with potassium hydroxide gave the BINOL dicarboxylic acid **53** which was then used to prepare the PIB-supported BINOL ligand **57** by the same coupling method discussed previously. A low molecular weight analogue of **57** was also prepared using this coupling method (cf. Scheme 42).



Scheme 41. Alternate synthesis of the 2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid **53.**



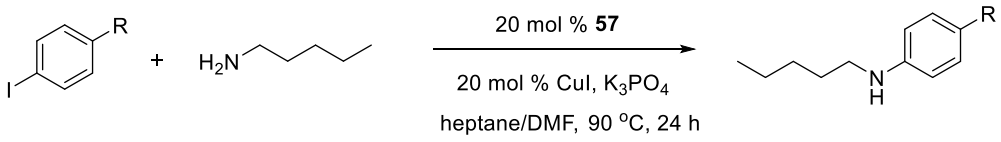
Scheme 42. Synthesis of the low molecular weight analogue **61** of PIB-supported BINOL ligand **57**.

After the racemic PIB-supported BINOL ligand **57** was prepared on a larger scale, it was then tested as a ligand for *N*-arylation reactions using copper iodide as shown in Scheme 43. Although we eventually wanted to use an enantiopure PIB-supported BINOL ligand in asymmetric catalysis, we first wanted to determine the activity of racemic **57**. Heptane/DMF was chosen as a thermomorphic solvent system for these *N*-arylation reactions which had previously been studied using DMF[117] or DMSO[118] as solvents when a racemic BINOL ligand was used. Copper iodide was chosen as the copper source because it is much more air stable than copper bromide, which was previously reported as a catalyst for this reaction.[117]

When we tested racemic BINOL as a ligand with copper iodide (20 mol % of both) in the reaction of 4-iodotoluene with amylamine using potassium phosphate as the base, a GC yield of 48% was obtained for the arylamine product after 24 h at 90 ^{o}C (cf. Table 11). This reduction in yield compared to previous reports may be due to the incorporation of heptane as a cosolvent with DMF. For instance, Fu reported that the reaction of 1-chloro-4-iodobenzene with amylamine using 5% copper bromide and racemic BINOL gave a

77% yield in DMF after 4 h but only a 12% yield in toluene, a similarly nonpolar solvent.[117]

When the PIB-supported BINOL ligand **57** was used under the same conditions with 4-iodotoluene and amylamine, a remarkably lower GC yield (3%) was obtained after 24 h which was comparable to using copper iodide without a ligand in the same system (2%). Surprisingly, when the low molecular weight analogue **61** was used with copper iodide in the reaction of amylamine and 4-iodotoluene at a six-fold higher concentration, a 35% GC yield was obtained after only 8 h. This suggests that increasing the concentration of the reaction may be able to increase the conversion to the arylamine. However, it is also possible that **61** is a more viable ligand for this reaction because it has significantly less steric hindrance around the hydroxyl groups than **57**, which contains a tertiary carbon next to the nitrogen of each amide group. In contrast, the nitrogen of each amide group of **61** is next to a primary carbon, lowering steric hindrance around the hydroxyl groups.



Scheme 43. *N*-arylation reactions of substituted arenes with amylamine using PIB-supported BINOL ligand **57** and copper iodide in a heptane/DMF thermomorphic system.

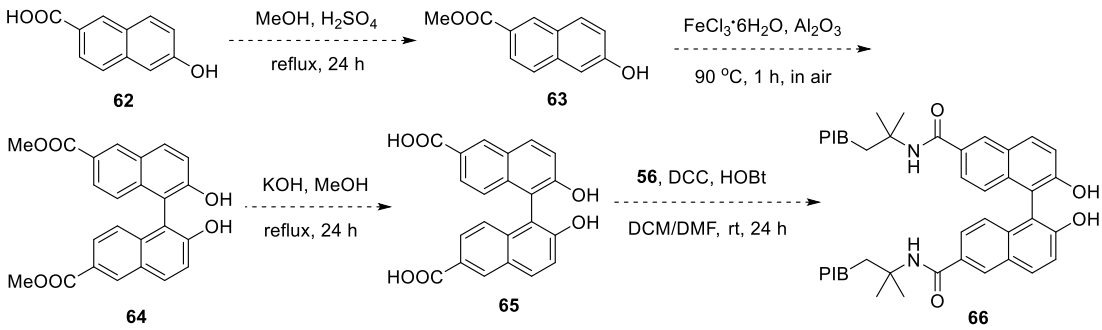
Table 11. *N*-arylation reactions using BINOL ligands with copper iodide.[a]

Substrate	Ligand	Base	Reaction Time (h)	GC Yield (%)
4-iodotoluene	BINOL	K_3PO_4	24	48
4-iodotoluene	**57**	K_3PO_4	24	3
4-iodotoluene[b]	**61**	K_3PO_4	8	35
4-iodotoluene	--	K_3PO_4	24	2
1-chloro-4-iodobenzene	**57**	K_3PO_4	24	11
1-chloro-4-iodobenzene	**57**	K_2CO_3	24	14

[a] 0.25 mmol of substrate, 0.38 mmol of amylamine, and 0.50 mmol of base were used with 0.05 mmol of copper iodide and 0.05 mmol of the ligand in 1.5 mL of heptane and 1.5 mL of DMF.
[b] This reaction was carried out using a six-fold higher concentration (0.92 mmol of substrate in 1 mL of heptane and 1 mL of DMF).

A more reactive starting material, 1-chloro-4-iodobenzene, was also allowed to react with amylamine using the PIB-supported BINOL ligand **57** and copper iodide. The GC yield remained low when using either potassium phosphate (11%) or potassium carbonate (14%) as the base. To optimize this reaction, other solvents such as THF should be tested and the concentration of the substrates should be increased although the solubility of the PIB-supported ligand in the solvent is a limitation for this. If an electronic effect is responsible for the decreased reactivity of the PIB-supported BINOL ligand **57** in comparison with BINOL, the amide groups of **57** can also be reduced to amine groups to see whether an increase in reactivity can be seen. To decrease the steric hindrance, the PIB-supported BINOL ligand **66** can also be prepared using a similar procedure, as shown in Scheme 44.

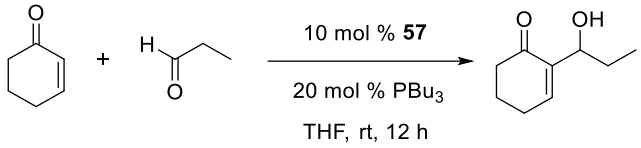
For this synthesis, 2-hydroxy-6-naphthoic acid can first be converted to the methyl ester **63** by esterification with methanol. This methyl ester **63** can then be used in an oxidative coupling reaction with iron (III) chloride hexahydrate on alumina to give the BINOL derivative **64** with methyl ester groups in the 6,6'-positions. Hydrolysis of **64** with potassium hydroxide can then give the BINOL dicarboxylic acid **65**. This BINOL dicarboxylic acid **65** can next be coupled with the amine-terminated PIB **56** to give the less sterically hindered PIB-supported ligand **66.**



Scheme 44. Proposed synthesis of the less sterically hindered PIB-supported BINOL ligand **66**.

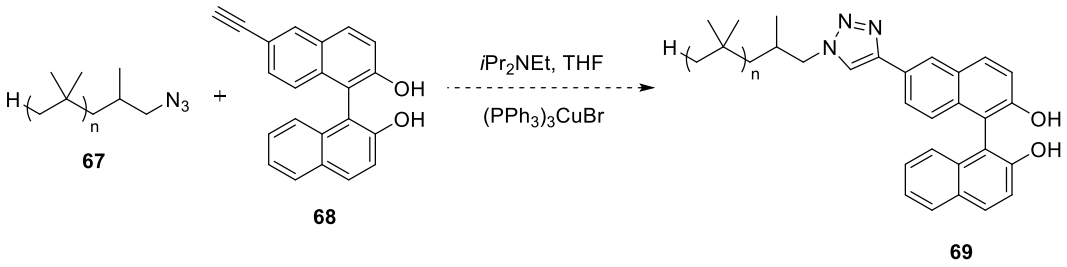
The PIB-supported BINOL ligand **57** (10 mol %) was also tested in the Baylis-Hillman reaction of 2-cyclohexen-1-one with propionaldehyde and tributylphosphine (20 mol %), as shown in Scheme 45. This reaction was previously reported by Ikegami using racemic BINOL and tributylphosphine.[119] While our experiments showed that a >99% yield by ^{1}H NMR spectroscopy of the product could be obtained when using racemic

BINOL as Ikegami reported for a similar reaction with 3-phenylpropanal and 2-cyclopenten-1-one,[119] use of the PIB-supported BINOL ligand **57** gave only a 24% yield, which is similar to the 23% yield reported for a control experiment Ikegami and coworkers carried out with only tributylphosphine in the absence of a ligand using the same substrates as the previous case. This further suggests that the PIB-supported ligand **57** is problematic, either due to a steric or electronic effect or a combination of both.



Scheme 45. Baylis-Hillman reaction of 2-cyclohexen-1-one with propionaldehyde using tributylphosphine and the PIB-supported BINOL ligand **57**.

Another synthesis that can be attempted for the preparation of a PIB-bound BINOL ligand that avoids a steric effect draws from literature previously reported by our group[120] as well as from Walsh and Pericas[107] and uses click chemistry originally reported by Sharpless.[121] For this synthesis, the azide-terminated PIB **67** could be prepared from bromide-terminated PIB using a known procedure from our group.[120] This azide **67** could then be allowed to react with 6-ethynyl-[1,1'-binaphthalene]-2,2'-diol **68** prepared using the synthesis reported by Walsh and Pericas[107], bromotris(triphenylphosphine) copper (I), and *N*,*N*-diisopropylethylamine to give the PIB-supported triazole product **69**, as shown in Scheme 46.



Scheme 46. Click coupling reaction of azide-terminated PIB **67** and 6-ethynyl-[1,1'-binaphthalene]-2,2'-diol **68**.

Conclusions

In this work, we were interested in synthesizing a PIB-supported BINOL ligand and testing its activity in catalytic reactions. An attempt to synthesize a PIB-supported BINOL ligand by the azo coupling of BINOL with the diazonium salt of 2,6-dimethyl-4-(polyisobutyl)aniline failed. Similarly, the Wittig reaction of a BINOL dialdehyde with phosphonium salt-terminated PIB was unsuccessful. Our third attempt to prepare a PIB-supported BINOL ligand by the coupling of achiral amine-terminated PIB with a BINOL dicarboxylic acid was successful. Two synthetic methods were developed for the preparation of this PIB-supported BINOL ligand **57**, and then its activity was tested in an *N*-arylation reaction with copper iodide and in a Baylis-Hillman reaction with tributylphosphine. Unfortunately, use of the PIB-supported BINOL ligand **57** did not show an increase in either reaction rate compared with using only copper iodide or tributylphosphine alone. However, a low molecular weight analogue of **57** showed enhanced activity in the *N*-arylation reaction compared to **57** when a higher concentration

for the reaction was used, which suggests that either concentration or steric hindrance has a role in the activity of BINOL ligands in *N*-arylation reactions. If the reduced reactivity of the PIB-supported BINOL ligand is due to steric hindrance of the tertiary carbon next to the nitrogen of the amide group, synthesis of the PIB-supported BINOL ligand **66** can be carried out to prevent this issue. Alternatively, click chemistry can also be used to prepare the PIB-supported BINOL ligand **69**.

CHAPTER V

EXPERIMENTAL SECTION

General Experimental

Poly(α-olefins) (PAOs) with molecular weights of 687, 1758, and 2505 Da were obtained from Dr. Wenning Han at Exxon Mobil. PAO_{687} had a Đ of 1.12 and a viscosity of 10 cSt. PAO_{1758} had a Đ of 1.35 and a viscosity of 40 cSt. PAO_{2505} had a Đ of 1.47 and a viscosity of 65 cSt. These PAOs had densities between 0.84-0.85 g/mL. The propylene-hexene copolymer **22** with a molecular weight of 800 Da was obtained from Baker-Hughes. Polyisobutylene (PIB) with reported molecular weights (M_n) of 1000 or 2300 Da was obtained either from BASF or Texas Polymer Corporation (TPC). MPEGs with reported M_n values of 750, 1000, 2000, and 5000 Da were obtained from Aldrich, Fluka, and INEOS. The INEOS samples were obtained from Dr. Mike Killough. Other reagents were purchased from commercial sources and used without further purification unless otherwise stated. ^{1}H NMR spectra were recorded on Inova and Mercury NMR spectrometers operating at 299.96 MHz and 499.59 MHz and the .fid files are included as a supplementary file with this dissertation. Chemical shifts are reported in ppm with reference to $CHCl_3$ at 7.26 ppm, DMSO at 2.50 ppm, and acetone at 2.05 ppm. ^{13}C NMR spectra were recorded on Inova NMR spectrometers operating at 75.43 MHz and 125.72 MHz. Chemical shifts are reported in ppm with reference to $CHCl_3$ at 77.0 ppm, DMSO at 39.5 ppm, and acetone at 206.7 ppm. Coupling constants are given in Hz and the spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), dd

(doublet of doublets), br (broad peak) and m (multiplet). Infrared spectra were recorded on a Shimadzu IRAffinity-1S FT-IR spectrophotometer. UV-Visible spectra were recorded using a Shimadzu UV-2600 UV-Visible spectrophotometer and a Cary 100 UV-Vis spectrometer. Fluorescence spectra were recorded using a Horiba Scientific Fluoromax-4 spectrofluorometer.

Syntheses and Experimental Procedures

PIB-(CH_2OH terminated). A previous procedure reported by our group was used for this synthesis.[120] In this case, alkene-terminated PIB (27.19 g, 27.2 mmol) was dissolved in 100 mL of hexanes. 10 M Boron dimethylsulfide was then added dropwise (0.91 mL, 9.1 mmol) to this alkene solution and the reaction was stirred for 24 h at room temperature. After 24 h, the reaction solution was cooled to 0 ^{0}C and 20 mL of ethanol, 6 mL of 4 M NaOH, and 4 mL of 35% hydrogen peroxide were added and the resulting reaction mixture was allowed to stir for 2 h after which 150 mL of water was added. The hexanes phase was separated and the aqueous phase was washed with hexanes (5 x 50 mL). The combined hexanes phase was then washed with water (3 x 25 mL), brine (1 x 25 mL), dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The product was obtained as a colorless oil in quantitative yield. The product obtained after concentration under reduced pressure contained traces of hexane. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.48 (dd, J = 5.5 Hz, 10.2 Hz), 3.32 (dd, J = 7.5 Hz, 10.2 Hz), 0.8-1.6 (m).

PIB-(CH_2Br terminated). A previous procedure reported by our group was used for this synthesis.[120] In this case, alcohol-terminated PIB (5.02 g, 4.9 mmol) was dissolved in 50 mL of DCM, the reaction flask was purged with nitrogen, and the solution was placed in an ice bath. Next methanesulfonyl chloride (1.2 mL, 15 mmol) was added dropwise, followed by triethylamine (2.2 mL, 15 mmol) and the solution was allowed to stir for 6 h. DCM was removed under reduced pressure using a rotary evaporator and the crude product was then dissolved in 50 mL of heptane and 50 mL of acetone. Lithium bromide (6.75 g, 78 mmol) was then added and the solution was refluxed at 80 ^{0}C for 48 h. After the reaction was complete, 100 mL of hexanes was added and the hexanes layer was washed with water (3 x 20 mL) and 90% aqueous ethanol (5 x 20 mL). The hexanes were removed under reduced pressure using a rotary evaporator to give the product as a colorless oil in 60% yield after drying under vacuum overnight. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.41 (dd, *J* = 4.5 Hz, 9.5 Hz), 3.27 (dd, *J* = 7.5 Hz, 9.5 Hz), 0.8-1.6 (m).

Cresol-terminated PIB. This procedure was modified from the literature procedure for the preparation of phenol-terminated PIB.[120] In this reaction, alkene-terminated PIB (11.24 g, 11.2 mmol) was dissolved in 110 mL of DCM. *ortho*-Cresol (12.04 g, 111.3 mmol) was added to the solution which was then purged with nitrogen. Next sulfuric acid (1.32 g, 13.5 mmol) was added and the solution was stirred for 5 h at room temperature. After the reaction was complete, the solvent was removed under reduced pressure using a rotary evaporator and the crude product was added to 200 mL of hexanes and washed with acetonitrile (4 x 50 mL) and saturated sodium bicarbonate (4 x 50 mL). The hexanes layer

was then dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator to give the product as an oil in 71% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09 (s, 1 H), 7.06 (d, 1 H, *J* = 8.5 Hz), 6.69 (d, 1 H, *J* = 8.5 Hz), 3.40 (bs, 1 H), 2.25 (s, 3 H), 0.8-1.8 (m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.2, 142.6, 128.8, 124.7, 122.5, 114.17, multiple poorly resolved peaks between 30-39 and 58-60, 16.1.

2,6-Dimethyl-4-(polyisobutyl)aniline. A previous procedure reported by our group was used for this synthesis.[64] In this case, alkene-terminated PIB (20.52 g, 20 mmol) and 2,6-dimethylaniline (24.24 g, 200 mmol) were added to a pressure vessel. After purging with nitrogen, aluminum chloride (4.10 g, 30 mmol) was added and the pressure vessel was quickly sealed. The reaction was then stirred for 4 d at 200 ^{0}C in a sand bath. After 4 d, the reaction mixture was poured into 150 mL of water and 200 mL of hexanes. The hexanes phase was then washed with 90% ethanol (6 x 50 mL), dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The resulting oil was then purified using gradient column chromatography (hexanes, DCM) to give the product in 64% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.93 (s, 2 H), 3.44 (s, 2 H), 2.19 (s, 6 H), 1.76 (s, 2 H), 0.8-1.5 (m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.0, 139.8, 126.1, 121.0, multiple poorly resolved peaks between 30-39 and 58-60.

Phase selective solubility studies of 1-[(2,6-Dimethyl-4-polyisobutylphenyl)azo]-2-naphthol (21). A PIB_{2300}-bound azo dye (0.03 g) prepared by following a reported

procedure[64] was dissolved in 3.0 g of heptane, PP, or a heptane-PP solvent mixture (2:1 wt:wt). After dissolution of the dye in the nonpolar solvent, 3.0 g of methanol was added and the biphasic solvent system was heated to 90 °C in a sand bath with stirring to miscibilize the nonpolar solvent with methanol. After heating, the solution was cooled to room temperature and a biphasic system was reformed. The methanol layer was analyzed by UV-Visible spectroscopy to determine leaching of the polymer azo dye.

1-[(2,6-Dimethyl-4-polyisobutyl)phenyl]azo-4-phenol (23). This procedure was modified from the synthesis of **24** (*vide infra*). Potassium *tert*-butoxide was used as the base instead of potassium carbonate. The product was purified after synthesis and extractions using column chromatography eluting initially with 10% ethyl acetate in hexanes and then with 20% ethyl acetate in hexanes to give a dark yellow oil in 57% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, 2 H, J = 9.0 Hz), 7.07 (s, 2 H), 6.92 (d, 2 H, J = 9.0 Hz), 5.28 (bs, 1 H), 2.36 (s, 6 H), 1.86 (s, 2 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 150.5, 148.6, 147.5, 130.2, 127.0, 124.4, 115.7, multiple poorly resolved peaks between 30-39 and 58-60, 19.5.

1-[(2,6-Dimethyl-4-polyisobutylphenyl)azo]-2-naphthol (24). A previous procedure reported by our group was used for this synthesis and the synthesis of the other PIB-supported azo dyes.[64] In this case, 2,6-dimethyl-4-(polyisobutyl)aniline (1.00 g, 0.89 mmol) was dissolved in 5.0 mL of DCM. The flask was purged with nitrogen and placed in an ice bath and boron trifluoride diethyl etherate (0.18 mL, 1.5 mmol) and isoamyl

nitrite (0.18 mL, 1.3 mmol) were added dropwise. The reaction solution was allowed to stir for 2 h at 0 ^{0}C and then the product was quickly washed with water and pipetted into a solution of 2-naphthol (0.38 g, 2.7 mmol) and potassium carbonate (0.49 g, 3.5 mmol) in DCM (20 mL) at 0 ^{0}C. This reaction was stirred overnight during which it gradually warmed to ambient temperature. After completion of the reaction, the solvent was removed under reduced pressure using a rotary evaporator and the crude product was added to 200 mL of hexanes. The hexanes phase was washed with water (1 x 60 mL) and 90% ethanol (5 x 60 mL), dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator to give the product as a red oil in 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, 1 H, *J* = 8.0 Hz), 7.72 (d, 1 H, *J* = 9.5 Hz), 7.63 (d, 1 H, *J* = 7.5 Hz), 7.55 (t, 1 H, *J* = 7.5 Hz), 7.38 (t, 1 H, *J* = 7.5 Hz), 7.18 (s, 2 H), 6.94 (d, 1 H, *J* = 9.5 Hz), 2.66 (s, 6 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 149.9, 139.0, 138.7, 133.8, 130.5, 129.7, 128.7, 128.5, 127.9, 127.7, 125.1, 124.9, 121.4, multiple poorly resolved peaks between 30-39 and 58-60, 21.0.

2,4-Bis[(2,6-dimethyl-4-polyisobutylphenyl)azo]-1,3-benzenediol (25). This procedure was modified from the synthesis of **24**. The crude product was purified using column chromatography first with hexanes and then with 6% ethyl acetate in hexanes to give a maroon oil in 43% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, 1 H, *J* = 10.0 Hz), 7.12 (s, 2 H), 7.09 (s, 2 H), 6.28 (d, 1 H, *J* = 10.0 Hz), 2.55 (s, 6 H), 2.50 (s, 6 H), 1.86 (s, 2 H), 1.83 (s, 2 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 182.4, 177.4, 150.4, 148.8,

142.7, 135.7, 131.6, 130.8, 130.2, 129.1, 127.6, 124.0, 120.6, multiple poorly resolved peaks between 30-39 and 58-60, 20.0, 19.9.

2,4,6-Tris[(2,6-dimethyl-4-polyisobutylphenyl)azo]-1,3,5-benzenetriol (26). This procedure was modified from the synthesis of **24**. The crude product was purified using column chromatography first with 30% ethyl acetate in hexanes and then with dichloromethane to give the product as a dark red oil in 41% yield. ^{1}H NMR (300 MHz, $CDCl_3$): 7.10 (s, 6 H), 2.54 (s, 18 H), 1.88 (s, 2 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 178.5, 150.0, 135.8, 130.1, 128.9, 127.5, multiple poorly resolved peaks between 30-39 and 58-60.

4-Hydroxy-3-[(2,6-dimethyl-4-polyisobutylphenyl)azo]-2-benzopyranone coumarin (27). This procedure was modified from the synthesis of **24**. The crude product was purified using column chromatography with 10% ethyl acetate in hexanes to give the product as a bright yellow oil in 38% yield. ^{1}H NMR (500 MHz, $CDCl_3$): 8.11 (d, 1 H, J = 8.0 Hz), 7.64 (t, 1 H, J = 7.0 Hz), 7.30 (m, 2 H), 7.14 (s, 2 H), 2.59 (s, 6 H), 1.85 (s, 2 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 177.7, 159.3, 154.4, 151.2, 135.7, 134.8, 130.0, 128.0, 126.7, 124.3, 122.1, 120.4, 117.5, multiple poorly resolved peaks between 30-39 and 58-60.

1-(2,4,6-Trimethylphenylazo)-2-naphthol. This procedure was modified from the synthesis of **24** using 2,4,6-trimethylaniline as the starting material. The product was

purified after synthesis using column chromatography with DCM as the eluent and was isolated as a red solid in 40% yield. mp 129-134 ^{0}C (lit. 127-131 ^{0}C).[122] ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 1 H, *J* = 8.5 Hz), 7.73 (d, 1 H), 7.63 (m, 1 H), 7.53 (m, 1 H), 7.38 (m, 1 H), 7.00 (s, 2 H), 6.95 (d, 1 H, *J* = 9.5 Hz), 2.60 (s, 6 H), 2.34 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4, 139.3, 137.5, 134.1, 130.9, 130.8, 129.0, 128.8, 128.0, 125.4, 125.0, 121.6, 21.3, 20.7.

PIB-supported *p*-methyl red azo dye (28). This dye had previously been coupled to a terminal hydroxyl group on a polyolefin oligomer using the acid chloride derivative of *p*-methyl red. To us, a Mitsunobu reaction proved more convenient. In this Mitsunobu reaction, a 100-mL round-bottomed flask was charged with a stir bar, 2.0 g (2 mmol) of alcohol-terminated PIB, 0.91 g (4 mmol) of *p*-methyl red, and 0.02 g (0.2 mmol) of DMAP. This mixture was then dissolved in 50 mL of DCM and cooled to 0 ^{o}C. To this solution, 0.82 g (4 mmol) of DCC was added and the resulting solution was stirred overnight. The suspension that formed was filtered, and solvent was removed under reduced pressure using a rotary evaporator. The crude product was purified via silica column chromatography (5% ethyl acetate in hexanes) to give 1.41 g (71%) of a viscous red liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 9.1 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 9.1 Hz, 2H), 4.19 (dd, *J* = 6.0 Hz, 10.5 Hz, 1H), 4.04 (dd, *J* = 7.6 Hz, 10.5 Hz, 1H), 3.12 (s, 6H), 0.97-1.65 (m). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 155.8, 152.9, 143.7, 125.7, 125.6, 125.6, 121.9, 111.6, multiple poorly resolved peaks between 30-39 and 58-60.

General procedure for UV-Visible spectroscopy experiments using polymer cosolvents with methanol. 20 mg of the polymer-supported azo dye **24** was added to heptane, a heptane/polymer solvent combination, or a pure polymer solvent (3.0 g) in a 20-mL scintillation vial. After the dye dissolved, methanol was added (3.0 g) and this thermomorphic mixture was stirred and heated at 100 ^{0}C until the biphasic solution became visibly a single phase (typically a few minutes). This solution was then cooled to room temperature. A biphasic mixture reformed on cooling. After sitting overnight, the biphasic mixture was centrifuged. Then the methanol layer was removed with a pipet and its absorbance was analyzed by UV-Visible spectroscopy to determine the percent leaching. The UV-Visible spectra were taken from 200 to 800 nm with a 0.5 nm sampling interval. Since the extinction coefficient for the azo dye **24** could not be measured in methanol because of **24**'s low methanol solubility, we used an extinction coefficient of 18417 cm^{-1} M^{-1} which was the extinction coefficient of 1-(2,4,6-trimethylphenylazo)-2-naphthol, a structurally analogous azo dye that was soluble in methanol.

General experimental procedure for studies of isomerization rates of 28 using UV-Visible spectroscopy. The PIB-supported *p*-methyl red dye **28** was dissolved in heptane or PAO_{687} to form a 1.5 x 10^{-5} M solution of the dye. This solution was then used to follow the rate of thermal isomerization of the dye to an equilibrium mixture of *E* and *Z* isomers in a UV-Visible spectrometer. This thermal isomerization was monitored using 100 scans, 100 seconds between scans, and a fast sampling speed (7 nm/s). Once the solution had reached equilibrium, the cuvette was removed from the UV-Visible spectrometer and

allowed to isomerize in room light for 12 h to a different *Z*-enriched *E*/*Z* mixture of **28**. This solution was then placed in the spectrometer and the isomerization was again followed by UV-Visible spectroscopy. A similar procedure was followed when studying the rate of carboxylic acid-promoted thermal isomerization of the dye to an equilibrium mixture of *E* and *Z* isomers using various concentrations of both a low and high molecular weight carboxylic acid. The rate of this isomerization was calculated from the slope of the first order plot obtained by plotting $\ln[(A_{eq}-A_t)/(A_{eq}-A_o)]$ versus time using the λ_{max} of 420 nm where A_{eq} is the absorbance at equilibrium, A_t is the absorbance at time t, and A_o is the absorbance at time 0.

General procedure for ^{1}H NMR Analysis of PAO leaching using PAOs and methanol or DMF. 3.0 g of the PAO solvent and 3.0 g of the polar solvent (methanol or DMF) were added to a centrifuge tube and stirred with heating at 100 ^{0}C until monophasic (a few minutes) and then cooled to room temperature. After sitting overnight, the sample was centrifuged and the polar solvent was pipetted into a separate centrifuge tube from the PAO. The polar solvent was then centrifuged again and then a drop of the polar solvent was added to $CDCl_3$ in an NMR tube for analysis. ^{1}H NMR spectra were taken at room temperature for DMF. A similar procedure was used for methanol but the spectra were taken at -30^{0}C to shift the -OH peak away from the PAO region. 200 scans were taken with an acquisition time of 2 s for each spectrum.

General procedure for ^{1}H NMR analysis of PAO leaching into MeCN. 3.0 g of the PAO solvent and 3.0 g of MeCN were added to a centrifuge tube and stirred with heating at 100 ^{0}C for 24 h and then cooled to room temperature. After sitting overnight, the sample was centrifuged and the MeCN phase was pipetted into a separate centrifuge tube from the PAO. The polar phase was then centrifuged again and then a drop of MeCN was added to $CDCl_3$ in an NMR tube for analysis. 200 scans were taken at ambient temperature with acquisition times of 3 s for PAO_{687} and 4 s for PAO_{1758} and PAO_{2505}. Integration as described above then afforded an estimate of PAO leaching into MeCN. It should be noted that carrying out this analysis in the same way after 48 h afforded similar leaching values.

General calculation of PAO leaching using a PAO and methanol. To calculate the amount of PAO in the polar phase, the integral for the signal of the -CH_3 methanol peak at δ 3.5 was set to 100. The total integral of the two satellite peaks was then assumed to be 1.08. Alternatively, the integral of the satellite peaks due to the ^{13}C naturally occurring in the methanol were measured. The total integral for the two satellite peaks was typically 0.97% of the central peak, slightly different than the expected 1.08% value. The total integral of the signals from the PAO region (δ 0.8 - 1.4) was then either measured or if no signals were detected, we estimated a value that could have been detected. We then calculated the mg of PAO in the methanol phase based on the number of protons in the solvent (3 for methanol), the amount of the solvent, and the expected number of protons in the PAO. We used the M_n values of the PAOs to estimate the average number of protons expected for the PAOs of M_n 687 Da (100), 1758 Da (254), and 2505 Da (360). The

percent of the original PAO that leached into the polar solvent was then calculated based on the mg of PAO that was found in the polar phase. The estimate of PAO leaching in Chapter II was based on a polar solvent peak that had an integral set at 100 that should have had two ^{13}C satellite peaks with a total integral of 1.08. A second calculation of PAO leaching based on the measured integrals of the observed ^{13}C satellite peaks was also carried out. While we believe this second approach is less accurate, the two calculations of the amount of PAOs that leached into the polar solvent generally gave leaching values that varied by <10%. The equation used to do these calculations is provided below.

$$\left[3\text{ g MeOH}\right]\left[\frac{\text{integral of PAO peaks (0.8-1.4 }\delta)}{\text{integral of MeOH satellite peaks}}\right]\left[\frac{\text{Hs in } {}^{13}CH_3OH}{\text{mole of } {}^{13}CH_3OH}\right]\left[\frac{\text{1 mole of } {}^{13}CH_3OH}{\text{33 g of } {}^{13}CH_3OH}\right]\left[\frac{\text{0.0108 g of } {}^{13}CH_3OH}{\text{1 g of } {}^{12}CH_3OH}\right]\left[\frac{\text{1 mole of PAO}}{\text{PAO Hs}}\right]\left[\frac{\text{g of PAO}}{\text{1 mole of PAO}}\right] = \text{g of PAO}$$

In this equation, the integral of the PAO signal and the integral of the ^{13}C satellite signals are experimental values calculated from the integral of the methanol peak which was set at 100. The number of protons in methanol (as an example of the polar solvent) and the PAO are calculated from the formula or molecular weight, respectively; the molecular weight of $^{13}CH_3OH$, $^{12}CH_3OH$, and the PAO are known; the theoretical amount of $^{13}CH_3OH$ in 1 g of CH_3OH is known; and the amount of methanol (3 g) is known. Similar calculations were carried out for DMF or MeCN. As noted above, the integral for the satellite peaks used in all of the polar solvents was either assumed to be 1.08% of the base peak or was the measured integral of the two satellite peaks.

Below is an example with PAO_{687} and methanol that assumes that the satellite peaks are 1.08% of the intensity of the $^{12}CH_3OH$ peak. 3 g of PAO_{687} was used with 3 g of $^{12}CH_3OH$. 0.05 is the integral of the PAO_{687} peaks from δ 0.8 - 1.4 and 1.08 is the

combined integral of the methanol satellite peaks. There are 3 protons in one mole of $^{13}CH_3OH$, and 1 mole of $^{13}CH_3OH$ contains 33 g of $^{13}CH_3OH$. There are 0.0108 g of $^{13}CH_3OH$ in 1 g of $^{12}CH_3OH$. 1 mole of PAO_{687} has 100 protons, and the molecular weight of PAO_{687} is 687 g/mol.

$$\left[\begin{array}{c}3\text{ g of}\\ \text{MeOH}\end{array}\right]\left[\frac{0.05}{1.08}\right]\left[\frac{3\text{ Hs}}{1\text{ mole of }{}^{13}CH_3OH}\right]\left[\frac{1\text{ mole of }{}^{13}CH_3OH}{33\text{ g of }{}^{13}CH_3OH}\right]\left[\frac{0.0108\text{ g of }{}^{13}CH_3OH}{1\text{ g of }{}^{12}CH_3OH}\right]\left[\frac{1\text{ mole of PAO}}{100\text{ Hs}}\right]\left[\frac{687\text{ g of PAO}}{1\text{ mole of PAO}}\right] = \text{g of PAO}$$

The result of this calculation is that there are 0.0010 g of PAO_{687} in the methanol phase, or 1.0 mg. Because the starting weight of the PAO was 3 g, the leaching percent can be calculated by 0.0010 g/3.0 g x 100, which gives a leaching value of 0.03%.

Mesylate-terminated PEG monomethyl ether (34). A previous procedure reported by our group was used for this synthesis.[91] In this case, to a solution of 5.0 g (2.5 mmol) of methoxy-terminated PEG in 15 mL of DCM was added 0.38 g (3.8 mmol) of triethylamine. This solution was then cooled to 0 ^{o}C and 0.43 g (3.8 mmol) of methanesulfonyl chloride was added. After stirring for 12 h at room temperature, the solution was added to an additional 60 mL of DCM and washed with 3 M HCl (3 x 20 mL), $NaHCO_3$ (3 x 20 mL), and brine (3 x 20 mL). The organic layer was separated, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator to give a pale yellow viscous oil in 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.40 (m, 2 H), 3.45-3.70 (m, 180 H), 3.38 (s, 3 H), 3.08 (s, 3 H).

4-Nitrophenyl-terminated PEG monomethyl ether (35). A procedure reported by Liu et al. was used for this synthesis.[89] In this case, 0.42 g (3.0 mmol) of *p*-nitrophenol was dissolved in 70 mL of acetone and then 0.69 g (5.0 mmol) of potassium carbonate was added and the solution was stirred for 1 h at room temperature. Then 5.00 g (2.50 mmol) of **34** was added and the solution was refluxed for 12 h. After cooling, the solvent was removed under reduced pressure using a rotary evaporator and the crude product was recrystallized in isopropanol to give the product in 25% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, 2 H, J = 9.3 Hz), 6.98 (d, 2 H, J = 9.3 Hz), 4.22 (m, 2 H), 3.99 (m, 2 H), 3.50-3.80 (m, 180 H), 3.38 (s, 3 H).

4-Aminophenyl-terminated PEG monomethyl ether (36). A procedure reported by Liu et al. was used for this synthesis.[89] In this case, a solution of 0.50 g (0.23 mmol) of **35** in 8 mL of methanol was prepared and 0.03 g (0.023 mmol) of 10% palladium on carbon was added before sealing the flask and purging three times with hydrogen gas. The flask was left under hydrogen and stirred for 24 h. Then the solution was filtered through Celite and the solvent was removed under reduced pressure using a rotary evaporator to give the product as an orange oil in 98% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.77 (d, 2 H, J = 8.9 Hz), 6.64 (d, 2 H, J = 8.9 Hz), 4.06 (m, 2 H), 3.50-3.85 (m, 180 H), 3.39 (s, 3 H).

PEG-supported naphthol azo dye (37). A procedure modified from that reported by Stein et al. was used for this synthesis.[88] In this case, a solution of **36** (7.95 g, 3.77 mmol) in 24 mL of water was prepared and 1.4 mL of 12 M HCl was added. The solution was

cooled to 0 °C and methanol was added until a clear solution was obtained. A precooled solution of 0.39 g (5.7 mmol) of sodium nitrite in water was added dropwise and the solution was stirred for 30 min at 0 °C. The pH of the solution was then adjusted to between 8-9 with a precooled solution of saturated sodium bicarbonate. Then 0.82 g (5.7 mmol) of 2-naphthol was added and the solution was stirred at 0 °C, gradually warming to room temperature over 12 h. Then the aqueous solution was washed with DCM (3 x 30 mL) and the combined organic fractions were washed with 10 mL of water and 10 mL of brine. The organic phase was dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The product was then recrystallized in isopropanol to give the product as a red solid in 43% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.71 (d, 1 H, J = 8.0 Hz), 7.83 (d, 2 H, J = 7.0 Hz), 7.76 (d, 1 H, J = 9.2 Hz), 7.70 (d, 1 H, J = 8.0 Hz), 7.58 (t, 1 H, J = 8.4 Hz), 7.41 (t, 1 H, J = 9.2 Hz), 7.05 (m, 3 H), 4.22 (m, 2 H), 3.5-4.1 (m, 180 H), 3.43 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 159.9, 141.9, 136.7, 133.3, 129.5, 128.3, 128.2, 128.1, 124.8, 122.2, 122.0, 121.6, 115.5, multiple poorly resolved peaks between 69-72, 67.8, 59.0. IR (neat, cm^{-1}) 2882, 1744, 1466, 1341, 1279, 1240, 1105, 961, 841.

General procedure for testing the removal of phenols by barium hydroxide. A solution of 1.13 g (1.33 mmol) of methoxy-terminated PEG_{750} in 50 mL of DCM was prepared and then 0.41 g (2.7 mmol) of *p*-nitrophenol and 0.91 g (5.3 mmol) of barium hydroxide were added. The suspension was allowed to stir at room temperature for 16 h, and then the precipitated barium salt of nitrophenol was filtered and the DCM removed

under reduced pressure using a rotary evaporator to isolate the methoxy-terminated PEG_{750}.

5-(Dimethylamino)-*N*-propylnaphthalene-1-sulfonamide (38). A procedure reported by Summers et al. was used for this synthesis.[90] In this case, 2.63 g (44.5 mmol) of *n*-propylamine was added to a solution of dansyl chloride (1.00 g, 0.370 mmol) in 50 mL of MeCN. The solution was allowed to stir at room temperature for 1 h and then the solvent was removed under reduced pressure using a rotary evaporator. The pale green solid obtained was then dissolved in 100 mL of DCM and washed with water (3 x 30 mL). The DCM phase was then filtered through 10 g of silica gel and the solvent was again removed under reduced pressure using a rotary evaporator. A 1:1 mixture of 95% aqueous ethanol and water was then added and the crude product was placed in an ice bath. The crystals obtained were then isolated by suction filtration to give the product in 60% yield. mp 98-100 ^{o}C (lit 86-88 ^{o}C).[90] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (d, 1 H, J = 8.8 Hz), 8.21 (m, 2 H), 7.49 (m, 2 H), 7.14 (d, 1 H, J = 6.4 Hz), 4.48 (m, 1 H), 2.85 (s, 6 H), 2.78 (m, 2 H), 1.43 (m, 2 H), 1.43 (m, 2 H), 0.75 (t, 3 H, J = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 134.7, 130.4, 129.9, 129.7, 129.6, 128.4, 123.2, 118.6, 115.1, 45.4, 43.0, 19.6, 13.4.

Dansyl-terminated PEG monomethyl ether (39). A previous procedure reported by our group was used for this synthesis.[91] In this case, a solution of 1.10 g (3.76 mmol) of **38** in 100 mL of DMF was prepared and 0.72 g (3.8 mmol) of cesium carbonate was added. After the solution was allowed to stir for 1 h, 5.03 g (0.990 mmol) of **34** was added and

the solution was refluxed at 90 ^{o}C for 96 h. Then 100 mL of water was added to the reaction solution and the water layer was washed with diethyl ether (3 x 100 mL) and DCM (3 x 80 mL). The DCM layers were combined and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was purified by either precipitation in diethyl ether or by column chromatography with 50% methanol in DCM as the eluent. The PEG_{2000}- and PEG_{5000}-supported dyes were obtained as solids and the PEG_{750}- and PEG_{1000}-supported dyes were obtained as viscous oils. (300 MHz, $CDCl_3$): δ 8.51 (d, 1 H, J = 8.5 Hz), 8.29 (d, 1 H, J = 8.5 Hz), 8.15 (d, 1 H, J = 7.5 Hz), 7.51 (m, 2 H), 7.18 (d, 1 H, J = 7.5 Hz), 3.5-3.7 (m), 3.37 (s, 3 H), 3.30 (m, 2 H), 2.89 (s, 6 H), 1.55 (m, 2 H), 0.76 (t, 3 H, J = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.6, 135.6, 130.1, 130.0, 130.0, 128.9, 127.9, 123.1, 119.7, 115.1, multiple poorly resolved peaks between 70-73, 61.7, 59.0, 50.4, 46.5, 45.4, 21.6, 11.0. IR (neat, cm^{-1}) 3462, 2884, 2860, 1466, 1341, 1279, 1240, 1103, 957, 841. Fluorescence data for **39** in various solvents is provided in Table 8.

General procedure for phase selectivity experiments with dansyl-terminated PEG monomethyl ether fluorophore 39. The dansyl-terminated PEG monomethyl ether dye **39** was added to a vial and dissolved in 3 g of DMF. Next 3 g of heptane was also added, and the solution was heated at 90 ^{o}C until a monophasic solution formed. After cooling overnight, the layers were centrifuged and the phases were separated using a pipet. The concentration of **39** in both phases was then determined by using a fluorimeter. To measure the DMF sample, 50 μL of the initial 3 g phase was added to a 50-mL volumetric flask (a dilution factor of 1000). The heptane phase was measured directly. Each fluorescence

measurement was done twice to ensure a consistent result. The excitation wavelength used for these emission spectra was 357 nm. The equation used to determine the leaching of **39** into the heptane layer is given below. This equation assumes that the extinction coefficients of **39** are equal in both solvents.

$$\frac{\text{fluorescence intensity of heptane layer}}{\text{fluorescence intensity of heptane layer} + \left[1000\right] \text{fluorescence intensity of DMF layer}}$$

2,2'-Bis(ethoxymethoxy)-1,1'-binaphthalene (52). A procedure reported by Yang et al. was used for this synthesis.[106] In this case, 1.40 g of 60% sodium hydride in mineral oil (34.9 mmol) was suspended in a mixture of 12 mL of anhydrous DMF and 28 mL of anhydrous THF at 0 ^{o}C. Next, 1.99 g of BINOL (6.95 mmol) in 8 mL of anhydrous THF was added dropwise and then the resulting suspension was stirred for 1 h at rt. Then 1.82 mL (21.0 mmol) of chloromethyl ethyl ether, a suspected carcinogen with acute inhalation toxicity, was added dropwise and the suspension was further stirred for 4 h at room temperature. The reaction was then quenched with water and the aqueous phase was washed with ethyl acetate (3 x 30 mL). The ethyl acetate layers were then combined and washed once with water (1 x 20 mL) and once with brine (1 x 20 mL). The organic layer was then dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The product was then recrystallized from 3:1 hexanes: DCM to give the product in 66% isolated yield as white crystals. mp 79-83 ^{o}C. ^{1}H NMR

(500 MHz, $CDCl_3$): δ 7.94 (d, 2 H, *J* = 9.0 Hz), 7.87 (d, 2 H, *J* = 8.0 Hz), 7.61 (d, 2 H, *J* = 9.0 Hz), 7.34 (t, 2 H, *J* = 7.5 Hz), 7.21 (t, 2 H, *J* = 8.0 Hz), 7.14 (d, 2 H, *J* = 8.5 Hz), 5.13 (d, 2 H, *J* = 7.0 Hz), 5.02 (d, 2 H, *J* = 7.0 Hz), 3.36 (m, 4 H), 1.00 (t, 6 H, *J* = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 134.0, 129.8, 129.3, 127.8, 126.2, 125.6, 124.0, 121.2, 117.4, 93.9, 63.9, 14.9. IR (neat, cm^{-1}) 2924, 1506, 1229, 1072, 1011, 802.

2,2'-Dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid (53). A procedure reported by Yang et al. was used for this synthesis.[106] In this case, 1.00 g (2.49 mmol) of **52** was dissolved in 5 mL of anhydrous THF and the flask was placed in an ice bath at 0 ^oC. Next, 3.6 mL (6.22 mmol) of 1.78 M *n*-butyllithium in hexanes was added dropwise and a dark solution ensued which became lighter and cloudier as the solution was allowed to stir for 2 h. Then several pellets of fresh dry ice were added and the suspension changed rapidly from yellow to white. This suspension was allowed to stir overnight and then the solution was quenched with water. This aqueous solution was washed once with diethyl ether (1 x 10 mL) and then acidified to pH 2 with 5% aqueous HCl. This acidic solution was then washed with ethyl acetate (3 x 50 mL). The ethyl acetate layers were combined, washed once with brine (1 x 10 mL), dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The crude protected product was then added to 4 mL of THF and 7 mL of saturated HCl in isopropanol which had been previously prepared by dropping concentrated sulfuric acid into sodium chloride and allowing the resulting hydrochloric acid gas to be purged into isopropanol. The solution was stirred for 2 h and then poured into 100 mL of ethyl acetate. The ethyl acetate

solution was washed with 10 mL of water, dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The resulting yellow solid was then crystallized in chloroform to give the product in 66% isolated yield. ^{1}H NMR (500 MHz, *d*-acetone) δ 10.99 (s, 2 H), 8.81 (s, 2 H), 8.08 (m, 2 H), 7.39 (m, 4 H), 7.13 (m, 2 H). ^{13}C NMR (125 MHz, *d*-acetone) δ 172.0, 154.8, 137.4, 133.0, 129.8, 129.2, 127.2, 124.5, 123.8, 117.1, 114.1. IR (neat, cm^{-1}) 3059, 2928, 2853, 1661, 1456, 1273, 1231, 735.

2,2'-Dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid (53). A modification of a procedure reported by Someshwar was used for this synthesis.[116] In this case, 1.98 g (4.93 mmol) of **60** (*vide infra*) was added to 100 mL of methanol and then 2.80 g of potassium hydroxide (49.9 mmol) was added and the solution was heated to reflux for 24 h. After this time, the reaction was cooled to room temperature and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was then dissolved in water and aqueous hydrochloric acid was added until the product precipitated as a yellow solid. The solid was filtered, washed with water, and dried to give the product in quantitative yield. The spectra obtained were identical to those reported previously using a different synthetic procedure.

Formamide-terminated PIB (55). 5.01 g (5.01 mmol) of alkene-terminated PIB was added to a 50-mL round-bottomed flask followed by trimethylsilyl cyanide (0.99 g, 10 mmol). Next 15 mL of DCM was added and to this reaction solution 0.48 mL of

concentrated sulfuric acid was added dropwise over 1-2 min. The solution was allowed to stir for 1 h, then water was added. The resulting solution was stirred overnight and then the DCM solvent was removed under reduced pressure using a rotary evaporator. The crude product was poured into 50 mL of hexanes and 35 mL of MeCN. The hexanes layer was then washed once more with sodium bicarbonate (20 mL) and the organic layer was dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The product was then purified by column chromatography with 10% diethyl ether in DCM as the eluent to give the product as a colorless oil (55/45 mixture of *re/si* isomers) in 53% isolated yield.

^{1}H NMR (500 MHz, $CDCl_3$): 8.23 (d, 1 H, J = 12.5 Hz), 5.69 (d, 1 H, J = 12.5 Hz), 5.23 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 162.6, 54.2, multiple poorly resolved peaks between 30-39 and 58-60.

^{1}H NMR (500 MHz, $CDCl_3$): 8.00 (d, 1 H, J = 2.0 Hz), 5.23 (s, 1 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 160.3, 53.6, multiple poorly resolved peaks between 30-39 and 58-60.

Amine-terminated PIB (56). 10.8 g (10.3 mmol) of **55** was added to 130 mL of hexanes and 90 mL of 90% aqueous ethanol. 10.3 g (234 mmol) of sodium hydroxide was then added and the solution was refluxed for 48 h. After cooling to room temperature, the biphasic mixture was poured into more hexanes in a separatory funnel, the layers were separated, and the hexanes layer was washed twice more with 90% ethanol (2 x 50 mL). The hexanes layer was then dried over sodium sulfate, filtered, and the solvent was

removed under reduced pressure using a rotary evaporator to give PIB amine as a pale yellow oil in 93% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$): 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 168.9, 51.5, multiple poorly resolved peaks between 30-39 and 58-60. IR (neat, cm^{-1}) 2949, 2893, 1472, 1389, 1366, 1231.

PIB-supported BINOL ligand (57). The amine-terminated PIB **56** (5.64 g, 5.54 mmol) was added to a 50-mL round-bottomed flask and dissolved in 10 mL of DCM. Then 0.83 g (2.2 mmol) of **53** in 10 mL of a DMF/DCM mixture was added dropwise to the solution of **56**. The flask was sealed and placed under nitrogen, and then DCC (1.14 g, 5.51 mmol) and hydroxybenzotriazole (0.2145 g, 1.590 mmol) were dissolved in a similar mixture of DCM/DMF and the solution of these two compounds was added dropwise to the reaction solution. The reaction was allowed to stir at room temperature for 24 h, then the reaction suspension was poured into 150 mL of hexanes and washed with 90% EtOH (2 x 50 mL) and MeCN (2 x 50 mL). The hexanes layer was then dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator. The crude product was purified by column chromatography using 5% ethyl acetate in hexane to give 2.37 g (1.00 mmol) of the product in 38% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$): 12.11 (s, 2 H), 8.02 (s, 2 H), 7.77 (d, 2 H, J = 7.5 Hz), 7.27 (m, 2 H), 7.12 (d, 2 H, J = 8.5 Hz), 6.64 (s, 2 H), 0.8-1.6 (m). ^{13}C NMR (125 MHz, $CDCl_3$): 169.2, 154.4, 136.0, 128.9, 128.4, 127.0, 126.9, 124.7, 123.7, 118.4, 117.6, 56.5, 53.5, multiple poorly resolved peaks between 30-39 and 58-60. IR (neat, cm^{-1}) 3387, 2949, 2893, 1651, 1526, 1472, 1387, 1366, 1229, 737.

Methyl 3-hydroxy-2-naphthoate (59). A procedure reported by Love et al. was used for this synthesis.[115] In this case, 1.07 g (5.69 mmol) of 3-hydroxy-2-naphthoic acid was added to 20 mL of methanol and then 5 drops of concentrated sulfuric acid were added. The solution was heated to reflux for 24 h and then it was cooled to room temperature. The solvent was removed under reduced pressure using a rotary evaporator and the crude product was added to 50 mL of diethyl ether. The ether layer was washed twice with water (2 x 25 mL) and once with sodium bicarbonate (2 x 25 mL). The ether layer was then dried over sodium sulfate, filtered, and the solvent was removed under reduced pressure using a rotary evaporator to give the product as a pale yellow solid in 93% isolated yield. mp 72-75 ^{o}C (lit 71-72 ^{o}C).[115] ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.43 (s, 1 H), 8.49 (s, 1 H), 7.80 (d, 1 H, *J* = 8.0 Hz), 7.68 (d, 1 H, *J* = 8.5 Hz), 7.50 (t, 1 H, *J* = 8.0 Hz), 7.31 (m, 2 H), 4.03 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 156.3, 137.9, 132.4, 129.2, 129.1, 127.0, 126.3, 123.9, 114.2, 111.7, 52.6.

Dimethyl 2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylate (60). A procedure reported by Love et al. was used for this synthesis.[115] In this case, 1.20 g (4.45 mmol) of iron (III) chloride hexahydrate was dissolved in 12 mL of acetone and then 4.58 g of alumina Brockman I Type 506C was added and the suspension was gently shaken for a minute. Then the acetone was removed under reduced pressure using a rotary evaporator and 0.90 g (4.43 mmol) of methyl 3-hydroxy-2-naphthoate in 12 mL of DCM was added to the iron chloride and alumina mixture. A dark green suspension immediately formed which was gently shaken before removing the DCM under reduced pressure using a rotary

evaporator. The solid mixture was then heated to 90 ^{o}C and stirred in an oil bath for 1 h in a flask open to air, then the flask was cooled to room temperature and 9 mL of methanol and 3 mL of concentrated phosphoric acid were added and the suspension was stirred for 5 min. Then the alumina was filtered and washed with DCM, and the DCM filtrate was collected and washed three times with water (3 x 25 mL) and once with brine (1 x 25 mL). The DCM layer was dried over sodium sulfate, filtered, and then the solvent was removed under reduced pressure using a rotary evaporator to give the product as a yellow solid in 41% isolated yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.71 (s, 2 H), 8.69 (s, 2 H), 7.92 (m, 2 H), 7.33 (m, 4 H), 7.15 (m, 2 H), 4.06 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 154.0, 137.1, 132.8, 129.7, 129.4, 127.1, 124.6, 123.9, 116.9, 114.1, 52.7.

2,2'-Dihydroxy-*N,N*'-dipentyl-[1,1'-binaphthalene]-3,3'-dicarboxamide (61). This procedure was modified from the synthesis of the PIB-supported BINOL ligand **57**. After the reaction, the product was precipitated from DCM along with dicyclohexylurea (DCU). Then the DCU was removed by multiple crystallizations from acetone to give the product in 35% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.93 (s, 2 H), 8.10 (s, 2 H), 7.81 (m, 2 H), 7.28 (m, 2 H), 7.12 (m, 2 H), 6.75 (m, 2 H), 3.50 (q, 4 H, J = 6.9 Hz), 1.70 (m, 4 H), 1.41 (m, 8 H), 0.95 (t, 6 H, J = 6.9 Hz).

General procedure for *N*-arylation reactions using PIB-supported BINOL ligand 57 and copper iodide. 4-iodotoluene (0.0556 g, 0.26 mmol), potassium phosphate (0.1085 g, 0.51 mmol), copper iodide (0.0103 g, 0.053 mmol), and the PIB-supported BINOL

ligand **57** (0.1257 g, 0.053 mmol) were added to a 10-mL Schlenk tube and the flask was evacuated and backfilled with nitrogen five times. Then anhydrous heptane (1.5 mL) and DMF (1.5 mL) were added. The flask was again quickly evacuated and backfilled with nitrogen, and then amylamine (0.05 mL, 0.43 mmol) and *n*-dodecane (0.05 mL, 0.22 mmol) as an internal standard were added. The flask was then allowed to stir at 90 ^{o}C for 24 h. After this time, an aliquot of the reaction solution (0.1-0.2 mL) was taken at elevated temperature and the aliquot was added to 2.0 mL of ethyl acetate. The cloudy suspension was centrifuged to give a clear solution which was analyzed by GC to determine the yield.

General procedure for Baylis-Hillman reactions using PIB-supported BINOL ligand 57 and tributylphosphine. The PIB-supported BINOL ligand **57** (0.2506 g, 0.10 mmol) was added to a 5-mL round-bottomed flask with 1 mL of THF. The flask was placed under nitrogen, and then 2-cyclohexen-1-one (0.10 mL, 1.04 mmol), propionaldehyde (0.22 mL, 3.79 mmol), tributylphosphine (0.05 mL, 0.20 mmol), and 3,5-dimethylanisole (0.03 mL, 0.21 mmol) as an internal standard were added. The reaction was stirred at room temperature for 12 h, then an aliquot of the reaction solution was taken and added to *d*-chloroform to analyze the percent conversion to the target product by ^{1}H NMR spectroscopy.

4-Chloro-*N*-pentylaniline. ^{1}H NMR (500 MHz, $CDCl_3$): 7.14 (d, 2 H, J = 9.0 Hz), 6.54 (d, 2 H, J = 9.0 Hz), 3.09 (t, 2 H, J = 7.0 Hz), 1.62 (m, 2 H), 1.38 (m, 4 H), 0.95 (t, 3 H,

J = 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 147.1, 129.0, 121.5, 113.7, 44.1, 29.3, 29.1, 22.5, 14.0.

4-Methyl-*N*-pentylaniline. ^{1}H NMR (500 MHz, $CDCl_3$): 7.00 (d, 2 H, *J* = 8.0 Hz), 6.56 (d, 2 H, *J* = 8.0 Hz), 3.09 (t, 2 H, *J* = 7.0 Hz), 2.25 (s, 3 H), 1.62 (m, 2 H), 1.38 (m, 4 H), 0.94 (t, 3 H, *J* = 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 146.3, 129.7, 126.2, 112.9, 44.3, 29.4, 29.3, 22.5, 20.3, 14.0.

2-(1-Hydroxypropyl)cyclohex-2-en-1-one. ^{1}H NMR (500 MHz, $CDCl_3$): 6.86 (t, 1 H, *J* = 4.2 Hz), 4.20 (q, 1 H, *J* = 6.9 Hz), 2.97 (d, 1 H, *J* = 6.9 Hz), 2.40 (m, 4 H), 1.97 (m, 2 H), 1.63 (m, 2 H), 0.89 (t, 3 H, *J* = 7.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 200.7, 146.0, 140.5, 73.0, 38.7, 29.1, 25.6, 22.5, 10.3.

CHAPTER VI

SUMMARY

In summary, the work in this dissertation focused on the study of thermomorphic solvent systems which are used as a method for the separation of phase selectively soluble polymer-supported catalysts from the products of a catalytic reaction. The incorporation of polymers as solvents or cosolvents in these systems was investigated, because such polymer solvents are less toxic and less volatile than the organic solvents typically used. First, a PIB-supported naphthol azo dye was synthesized and used as a surrogate for a PIB-supported catalyst in a thermomorphic system of heptane and methanol. When this PIB-supported dye was used, the addition of poly(α-olefins) (PAOs) as cosolvents with heptane reduced the leaching of the dye into the methanol phase. When PAOs were used as replacements for heptane, the leaching of the dye into the polar methanol phase was decreased even further. 1.1% or less leaching of the dye into the polar phase was observed by UV-Visible spectroscopy when the PAOs were used as nonpolar solvents compared to the 4.1% value obtained by using heptane. The PAO with a molecular weight of 687 Da (PAO_{687}) was shown to be the most effective polymer solvent in reducing leaching of the PIB-supported dye into the polar phase. When PAO_{687} was used, it did not appreciably leach into the polar phase (<0.3% by ^{1}H NMR), alleviating the concern that the products would be significantly contaminated in a catalytic system and would require further purification. The PAOs were also easily recycled in thermomorphic systems with methanol because of their nonvolatility and their low leaching into the polar phase.

Phase selectivity studies were also conducted using a PEG-supported dansyl fluorophore as a catalyst surrogate in a heptane/DMF thermomorphic system. These studies showed that while the leaching of this PEG-supported dansyl dye into the heptane phase of this system was always low, when higher molecular weight polymer supports (2000 Da and 5000 Da) were used, a reduction in leaching was observed in comparison with the use of a lower molecular weight polymer support (750 Da). The addition of a PEG monomethyl ether (MPEG) polymer cosolvent with DMF did not reduce leaching of the PEG-supported dansyl dye into the heptane phase. Instead, the leaching of PEG-supported dansyl fluorophores with polymer supports of 1000 Da, 2000 Da, and 5000 Da was unaffected. This suggested that while MPEG does not serve as an "anti-leaching" agent like a PAO, it could still serve as a suitable polymer cosolvent for thermomorphic systems with heptane and DMF. The addition of $MPEG_{750}$ also slightly decreased the leaching of DMF into heptane as evidenced by ^{1}H NMR studies. This could be useful in preventing solvent loss of the DMF phase during recycling of this thermomorphic system if the MPEG does not significantly leach into the nonpolar phase.

Finally, a heptane phase selectively soluble BINOL ligand was synthesized by the coupling reaction of amine-terminated PIB and 2,2'-dihydroxy-[1,1'-binaphthalene]-3,3'-dicarboxylic acid. This ligand was then tested with copper iodide in *N*-arylation reactions. However, it showed substantially lower activity than its low molecular weight analogue or racemic BINOL. Further modification of the reaction conditions could make this a more promising synthesis, but these initial studies suggest that synthesizing a ligand from 2,2'-dihydroxy-[1,1'-binaphthalene]-6,6'-dicarboxylic acid instead of 2,2'-dihydroxy-[1,1'-

binaphthalene]-3,3’-dicarboxylic acid to avoid any effect due to steric hindrance would be a better alternative. The synthesis of a PIB-supported BINOL ligand using click chemistry is also a viable option.

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